



Developing a non-pharmacological intervention model to improve function and participation in people with primary Sjögren's syndrome

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**This dissertation is submitted for the degree of Doctor of Philosophy
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This thesis is dedicated to my family; Simon, Daniel, Sam and Grace

“I wake up each day hoping a treatment is developed that will allow me to live an active and normal life again”

Person with Sjögren’s syndrome (Sjögren's Syndrome Foundation, 2016)

“The primary goal of occupational therapy is to enable people to participate in the activities of everyday life. Occupational therapists achieve this outcome by working with people and communities to enhance their ability to engage in the occupations they want to, need to, or are expected to do, or by modifying the occupation or the environment to better support their occupational engagement.”

(World Federation of Occupational Therapists, 2012)

Declaration

This dissertation is the result of my own work and includes nothing, which is the outcome of work done in collaboration except where specifically indicated in the text. It has not been previously submitted, in part or whole, to any university or institution for any degree, diploma, or other qualification.

In accordance with the Faculty of Medical Sciences guidelines, this thesis does not exceed 80,000 words.

Signed: _____

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Abstract

Background:

Primary Sjögren's syndrome (PSS) is an autoimmune disease which primarily targets secretory glands causing sicca/dryness symptoms. Patients with PSS also experience a range of other symptoms including fatigue, pain, sleep disturbances, low mood and anxiety. These symptoms impact on activities of daily living, participation and quality of life. PSS has been an under researched disease, and as a consequence many needs of patients remain unmet within clinical settings.

Aim:

To design a non-pharmacological intervention strategy for people with PSS focussing on patient-relevant targets in order to improve daily function and participation.

Methods:

In this project, I use a mixed methods approach. I conducted a systematic review of published interventions of non-pharmacological interventions for PSS. Then concept mapping, a participatory mixed methods approach, was used to identify factors which interfere with performance of daily activity for people with PSS. These results were discussed with a steering group and used as a basis to develop an intervention strategy. I then conducted focus groups with patients and their spouses to discuss the main factors deemed to interfere with activities, ascertain strategies patients use to manage these problems, and to determine the acceptability of potential future interventions to address these factors. Finally a model for the delivery of non-pharmacological interventions to address these factors was developed with patients.

Results:

The systematic review found there was insufficient published evidence to either support or refute non-pharmacological interventions for PSS. The concept mapping study revealed that in addition to dryness; fatigue, pain and sleep disturbances were priority targets for future interventions. The qualitative focus groups demonstrated that patients currently deploy a range of strategies to self-manage fatigue, sleep and

pain. However, these strategies are not always successful and patients require individualised therapies which target their own priorities and required level of support.

Conclusion:

The work within this thesis provides a comprehensive understanding of factors which influence daily function and participation in PSS patients. This work presents a stakeholder-informed model for delivering future non-pharmacological interventions to address stakeholder informed priorities. As such, a model has been developed which will ultimately support patients to manage symptoms of fatigue, sleep disturbances and pain, which are perceived by patients, their families and health professionals to impact on performance of daily activities and participation.

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List of Abbreviations and Acronyms

ACT - Acceptance and commitment therapy

ACR - American College of Rheumatology

ADL - Activities of daily living

AECG - American European Consensus Criteria

AHM - Adult household members

AIMS - Arthritis Impact Measurement Scale

CBT - Cognitive behavioural therapy

CCRN NIHR - Comprehensive Clinical Research Network

CDSR - Cochrane Database of Systematic Reviews

CENTRAL - Cochrane Central Register of Controlled Trials

CFS - Chronic fatigue syndrome

COMPASS - Composite Autonomic Symptoms Scale

COPM – Canadian Occupational Performance Measure

CMOP – Canadian Model of Occupational Performance

CSI - Caregiver Strain Index

CRP - C-reactive protein

EQ-5D - European Quality of life Five Dimensions

ESSDAI - EULAR Disease Activity Index

ESSPRI - EULAR Sjögren's Syndrome Patient Reported Index

ESR - Erythrocyte sedimentation rate

EULAR - European League Against Rheumatism

GCM - Group concept mapping

GET - Graded exercise therapy

HADs - Hospital Anxiety and Depression Scale

HCP - Health care professionals

ICF - International Classification of Functioning, Disability and Health

IQR - Interquartile range

Improved HAQ - Improved Health Assessment Questionnaire©

MALT - Mucosal-associated lymphoid tissue

MDS - Multi-dimensional scaling

MRC - Medical Research Council

MeSH - Medical Sub Headings

NIHR - National Institute for Health Research

NRR - National Research Register Archive

PIC - Patient Identification Centres

PIs - Principal Investigators

PROFAD - Profile of Fatigue and Discomfort

PSS - Primary Sjögren's syndrome

RCT - Randomised controlled trial

SCAI - Sjögren's systemic Clinical Activity Index

SD - Standard deviation

SLE - Systemic lupus erythematosus

SS - Sjögren's syndrome

SSA - Antibodies to Ro Sjögren's syndrome antigen A

SSB - Sjögren's syndrome antigen B

SSDI - Sjögren's Syndrome Damage Index

SSI - Sicca Symptoms Inventory

TENS - Transcutaneous electrical nerve stimulation

VAS - Visual analogue scale

WHO - World Health Organisation

WHO ICTRP - World Health Organisation International Clinical Trials Registry Platform

US - United States

Chapter 1. Introduction

1.1 Introduction to the thesis

I have a clinical background in rheumatology occupational therapy and chronic fatigue syndrome (CFS). Whilst attending a research symposium in fatigue at Newcastle University in 2011, I heard Professor Ng give a presentation on fatigue in primary Sjögren's syndrome (PSS). PSS is a disease which is usually diagnosed and managed in rheumatology departments. However, despite the eight years I spent working in rheumatology departments, I could only recall seeing one patient with this condition. The years I spent working with CFS patients highlighted to me the debilitating impact chronic fatigue has on people's ability to carry out their daily activities and maintain their life roles. If people with CFS struggled to function and if PSS patients experienced a similar type of fatigue; then I hypothesised that they might also experience functional difficulties. This led to the collection and analysis of pilot data, which I conducted prior to starting my PhD and is discussed later in this chapter (see Section 1.5.2).

In this thesis, I use mixed methods research to identify factors which interfere with people with PSS from being able to conduct their daily activities. The methods I use include a systematic review of the literature, group concept mapping (Trochim, 1989), clinician involvement and qualitative focus groups.

1.2 Researcher perspective

I am an occupational therapist and I subscribe to the primary goal of occupational therapists stated in the quote in the front pages:

The primary goal of occupational therapy is to enable people to participate in the activities of everyday life. Occupational therapists achieve this outcome by working with people and communities to enhance their ability to engage in the occupations they want to, need to, or are expected to do, or by modifying the occupation or the environment to better support their occupational engagement. (World Federation of Occupational Therapists, 2012)

This philosophical standpoint will inevitably have affected the way I have conducted the research described in this thesis. In my clinical role, my primary goal is to see my patients being able to participate in activities of everyday life, regardless of their physical, cognitive or mental health impairments. Whilst conducting the research described in this thesis, I had the same ultimate goal in mind for people with PSS.

Before beginning my PhD study, I was a senior occupational therapist working with people with long term conditions. I have worked clinically for sixteen years in rheumatology and chronic fatigue syndrome (CFS) services. Whilst I was familiar with working with patients who experienced chronic fatigue and pain within the context of their rheumatic disease or CFS, I assumed that PSS patients experience dry eyes and mouth without any other accompanying symptoms. However, after hearing Professor Fai Ng (my primary supervisor) present his work in 2011, I realised that this disease had many other features, which appeared to be potentially quite disabling, including chronic fatigue. Consequently, I started to question why these patients seemed to rarely be referred to occupational therapy services (Hackett *et al.*, 2012a; Hackett *et al.*, 2012b) and started my research journey by investigating the difficulties that these patients can experience on a daily basis.

1.3 Background

PSS is a systemic autoimmune disease characterised by dryness (*sicca*) symptoms. It falls under the umbrella of connective tissue diseases and is usually diagnosed and treated by rheumatologists. In PSS, the body attacks its own secretory glands. Lymphocytes infiltrate these exocrine glands causing inflammation and damage over time. Consequently, people with the disease experience dryness, particularly in the eyes and mouth. These clinical features are visible during medical examination. However, there are further extra-glandular manifestations commonly experienced by people with PSS, which are less visible. These include pain (Segal *et al.*, 2013; Segal *et al.*, 2014; Koh *et al.*, 2016), fatigue (Bardsen *et al.*, 2016; Howard Tripp *et al.*, 2016; Karageorgas *et al.*, 2016) and low mood (Westhoff *et al.*, 2012). There can also be systemic involvement in PSS and this may affect any organ resulting in manifestations such as vasculitis, neuropathy as well as skin, lung and kidney involvement (Seror *et al.*, 2015).

1.3.1 History of Sjögren's syndrome

Sjögren's syndrome is named after Henrik Sjögren, a Swedish ophthalmologist who first described the condition (Sjögren, 1933). However, others including Henri Gougerot, a French dermatologist and Jan Mikulicz-Radecki, an Austrian/Polish surgeon had previously described cases which are likely to be Sjögren's syndrome in 1926 and 1892 respectively (Bowman, 2016).

1.3.2 Prevalence

A recent meta-analysis has identified a PSS prevalence rate of 65 per 100,000 inhabitants and a female to male ratio incidence of 9.15 to 1 (Qin *et al.*, 2015). It is thought to be one of the more common autoimmune rheumatic diseases (Holdgate and St Clair, 2016).

1.3.3 Secondary Sjögren's syndrome

Secondary Sjögren's syndrome can occur in conjunction with other autoimmune rheumatic diseases such as systemic lupus erythematosus, scleroderma or rheumatoid arthritis. Secondary Sjögren's syndrome shares some of the clinical features of PSS that I describe next. However, in this thesis I focus on Sjögren's syndrome, which occurs in isolation to these other diseases. I therefore continue to refer to it as 'primary' Sjögren's syndrome.

1.3.4 Age of onset

There are two main age peaks when PSS tends to develop. These are during the 20's to 30's and in the 50's following menopause (Fox, 2005). Qin *et al.*'s (2015) recent meta-analysis found the average age of onset to be 52.

1.3.5 Diagnosis

Currently, the most widely accepted criteria for PSS are the American-European Consensus Group (AECG) criteria (Vitali *et al.*, 1996) (see Table 1-1). More recently, an American College of Rheumatology (ACR) – European League Against Rheumatism (EULAR) criteria has been proposed (Shiboski *et al.*, 2012; Shiboski *et al.*, 2017). It is likely that the two criteria describe largely an overlapping population.

Classification for primary Sjögren's syndrome, adapted from Vitali et al. (2002)
<p>I. Ocular symptoms: a positive response to at least one of the following questions:</p> <p>Have you had daily, persistent, troublesome dry eyes for more than 3 months?</p> <p>Do you have a recurrent sensation of sand or gravel in the eyes?</p> <p>Do you use tear substitutes more than 3 times a day?</p> <p>II. Oral symptoms: a positive response to at least one of the following questions:</p> <p>Have you had a daily feeling of dry mouth for more than 3 months?</p> <p>Have you had recurrently or persistently swollen salivary glands as an adult?</p> <p>Do you frequently drink liquids to aid in swallowing dry food?</p> <p>III. Ocular signs—that is, objective evidence of ocular involvement defined as a positive result for at least one of the following two tests:</p> <p>Schirmer's I test, performed without anaesthesia (<5 mm in 5 minutes)</p> <p>Rose bengal score or other ocular dye score (>4 according to van Bijsterveld's scoring system)</p> <p>IV. Histopathology: In minor salivary glands (obtained through normal-appearing mucosa) focal lymphocytic sialoadenitis, evaluated by an expert histopathologist, with a focus score >1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4mm² of glandular tissue</p>

Table 1-1 The American-European Consensus Group PSS classification criteria, from Vitali et al. (2002)

Classification for primary Sjögren's syndrome, adapted from Vitali et al. (2002)

V. Salivary gland involvement: objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests:

Unstimulated whole salivary flow (<1.5 ml in 15 minutes)

Parotid sialography showing the presence of diffuse sialectasias (punctate, cavitary or destructive pattern), without evidence of obstruction in the major ducts¹⁹

Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer

VI. Autoantibodies: presence in the serum of the following autoantibodies:

Antibodies to Ro(SSA) or La(SSB) antigens, or both Anti-Ro/La antibodies or an inflammatory focus score on lip gland biopsy > or =1

AND

4 out of 6 of:

Dry eye symptoms

Dry mouth symptoms

Objective oral dryness (unstimulated salivary flow rate < or = 0.1ml/min) or positive salivary scintigraphy and sialography

Objective ocular dryness (Schirmer's test < or = 5mm in 5 mins/*van Bijsterveld score* >=4)

Positive Anti-Ro/La antibodies

Labial gland focus score > or =1

In patients without any potentially associated disease, PSS may be defined as follows:

a. The presence of any 4 of the 6 items is indicative of PSS, as long as either item IV (Histopathology) or VI (Serology) is positive

b. The presence of any 3 of the 4 objective criteria items (that is, items III, IV, V, VI)

1.3.6 Burden of PSS

There are significant direct and indirect health-related costs associated with the disease. Direct health care costs have been estimated at £1831 to £2546 per PSS patient per year in the UK, which is approximately 80% of the cost associated with rheumatoid arthritis (RA) in the era preceding widespread use of biological therapy for (RA) (2004-2005) (Callaghan *et al.*, 2007). Indirect costs in the UK are between 69%-83% of those associated with a patient with RA, and equate to £7677 to £13502 per PSS patient per year (Bowman *et al.*, 2010). This is supported by data gathered in the Netherlands, Germany and the USA, which demonstrates that PSS patients are significantly less likely to be in gainful employment, and are more likely to work reduced hours, be in receipt of benefits, and access health care services more frequently (Meijer *et al.*, 2009; Segal *et al.*, 2009; Westhoff *et al.*, 2012).

1.3.7 Treatment recommendations for PSS in the United Kingdom

Current treatments for PSS are limited. Pharmacological treatments tend to focus on topical treatments for dryness or oral muscarinic agonists which increase tear production and salivary flow (Moreland, 2004; Ramos-Casals *et al.*, 2010). However new national treatment guidelines for PSS should be published for the first time in the very near future (Price, 2016a; Price *et al.*, 2016). These guidelines make use of available published evidence and expert opinion. Within these guidelines are recommendations for specific topical and systemic treatments. There is also one non-pharmacological recommendation, which recommends graded exercise for PSS fatigue. However, as these recommendations are not yet published, it will be some time before the impact of the recommendations can be measured, in terms of widespread implementation in clinical practice.

1.3.8 Research into PSS

Compared to most other rheumatological autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus (SLE), there has been little research and intervention attention into PSS (Fox, 2005). For instance, I conducted a literature search in October 2016 using PubMed Central. When I used the search term 'primary Sjogren's syndrome', 4486 articles were revealed. In contrast, when I used the search

term 'rheumatoid arthritis', 129645 articles were revealed and my search for 'systemic lupus erythematosus' retrieved 63439 articles. This simple search illustrates the limited research into this condition; especially when the prevalence rates, the health economic impact of the disease and the fact that there is currently no effective treatment are taken into account.

In recent years, the limited clinical trials of drug treatments, did not demonstrate benefit over placebo. The majority of these trials have focussed on the sicca features, despite a range of symptoms experienced by PSS patients. Whilst there is some evidence from controlled trials of the benefits of pharmacological agents such as pilocarpine and cevimeline (both oral muscarinic agonists), as well as topical cyclosporine for moderate and severe dry eyes; anti-tumour-necrosis factor drugs have not been shown to be efficacious at improving joint pain, fatigue and dryness (Ramos-Casals *et al.*, 2010). The results of recent rituximab and belimumab trials (both b-cell targeted therapies) have also failed to meet their primary outcomes (30% reduction in 2 or more 10cm visual analogue scale (VAS) scores for global disease, fatigue, pain and dryness at 28 weeks following the start of treatment) (Devauchelle-Pensec *et al.*, 2014; Mariette *et al.*, 2015). Furthermore, a large trial of hydroxychloroquine also failed to demonstrate improvements in dryness, pain and fatigue at 24 weeks (Gottenberg *et al.*, 2014).

Although there has been limited research into pharmacological interventions and limited pharmacological treatment options (Birt *et al.*, 2017), there have been even fewer studies investigating non-pharmacological interventions. However, a systematic review of the literature into non-drug interventions has not previously been conducted. Therefore, it was important to conduct such a review to determine whether there are currently any known efficacious non-drug interventions, which may improve quality of life in PSS patients (see Chapter 2).

1.3.9 The United Kingdom Primary Sjögren's Syndrome Registry

The United Kingdom Primary Sjögren's Syndrome Registry (UKPSSR) was set up in Newcastle upon Tyne in 2011 with Medical Research Council (MRC) funding in order to facilitate high quality research into PSS (Ng *et al.*, 2011). Patients are recruited to the UKPSSR from centres across the UK and all participants fulfil the AECG classification

criteria. All participants have indicated whether they would like to take part in further studies into PSS. The UKPSSR is hosted in Newcastle upon Tyne. Newcastle is therefore the ideal place to conduct this PhD research, as there is a well-defined clinical cohort of patients who have consented to being contacted for further research, including the studies reported within this thesis.

1.3.10 Symptoms of PSS

There is a range of symptoms experienced by people with PSS. These symptoms have a huge impact on quality of life (Lendrem *et al.*, 2014; Cornec *et al.*, 2017), and can affect patients' ability to participate fully in life and to independently carry out a range of functional activities of daily living (Hackett *et al.*, 2012a; Hackett *et al.*, 2012b). In this section, I provide a brief summary of these symptoms and in the following section, I give an indication on the impact of these symptoms on daily function and participation.

1.3.11 Dryness

1.3.11.1 Oral dryness

Impaired function of the exocrine glands results in oral dryness or xerostomia (Ng and Bowman, 2010). Xerostomia may result in oral infections including candidiasis, oral lesions, enlargement of the salivary glands and dental caries (Yan *et al.*, 2011; Castro *et al.*, 2013; Likar-Manookin *et al.*, 2013; Gonzalez *et al.*, 2014; Napenas and Rouleau, 2014).

1.3.11.2 Ocular dryness

PSS patients regularly experience a moderate to severe aqueous-deficient form of dry eye due to a destructive autoimmune response in the lacrimal glands (Coursey and de Paiva, 2014). Ocular dryness, also known as keratoconjunctivitis sicca, can result in varying levels of symptoms, such as burning, photophobia, foreign body sensation, grittiness, and redness, and corneal ulceration (Benelli, 2011).

1.3.11.3 Other forms of dryness

Vaginal dryness and dyspareunia occur more frequently in women with PSS compared to controls (Cirpan *et al.*, 2007). Dryness of the airways may also contribute towards

the development of chronic cough in some PSS patients (Fairfax *et al.*, 1981; Flament *et al.*, 2016).

1.3.12 Vasculitis

Skin vasculitis is one of the most common extraglandular features of PSS with palpable purpura and leukocytostlastic vasculitis on pathological examination (Scofield 2011). Cutaneous vasculitis is usually a self-limiting condition which is more likely to affect small vessels, although it can also affect medium-sized vessels and cause erythematous papules (Ng *et al.*, 2016). Furthermore, Raynaud's phenomenon is common in PSS patients (Horvath *et al.*, 2014).

1.3.13 Internal organ involvement

PSS is a systemic disease, which can affect other organs including the kidneys, liver and lungs (Mavragani and Moutsopoulos 2010a). Although severe renal involvement is uncommon, interstitial nephritis can occur due to lymphocytic infiltration and this may result in renal tubular acidosis (Ng *et al.*, 2016). Pancreatitis is also more common in PSS (Ebert, 2012; Terzin *et al.*, 2012), with serious pancreatic complications occurring in 1% of patients (Price, 2016b).

1.3.14 Gastrointestinal disease and symptoms

Patients with PSS may experience a range of gastrointestinal symptoms. This may be due to a reduction in mucous in the gastrointestinal tract. PSS patients are more likely to experience gut motility problems (Bengtsson *et al.*, 2011) and may experience gastrointestinal disease including dysphagia, pancreatitis, pernicious anaemia and autoimmune hepatitis; as well as symptoms of irritable bowel syndrome including diarrhoea, abdominal pain, bloating and nausea (Ebert, 2012; Kim-Lee *et al.*, 2015). Coeliac disease is also present in up to 4.5% of PSS patients (Price, 2016b), which is higher than the 0.5% incidence in the general population (Feighery, 1999).

1.3.15 Lymphoma

A further complication of PSS includes an increased risk of the development of lymphoma (Rua-Figueroa *et al.*, 2016), particularly mucosal-associated lymphoid tissue (MALT) lymphomas (Lazarus *et al.*, 2006). PSS patients have a 15-20 fold increased risk

of developing lymphoma compared to the general population (Theander *et al.*, 2006), and the relative risk of lymphoma development in PSS is among the highest of all autoimmune diseases (Dong *et al.*, 2013). Therefore, careful monitoring of those at risk of developing lymphoma is essential. Recent research by colleagues at Newcastle University has identified potential biomarkers, (Al-Ali *et al.*, 2014; Tarn *et al.*, 2014) which in the near future could identify these susceptible individuals in a clinical setting. This raises the question – should all PSS patients follow the same treatment pathway? Perhaps an alternative pathway could be available to the majority of patients who are at much lower risk of developing lymphoma.

1.3.16 Neurological features

1.3.16.1 Peripheral neuropathy

The nervous system is affected in approximately 20% of people with PSS (Chai and Logigian, 2010; Tobon *et al.*, 2012) and 5-15% of patients have peripheral neuropathy (Birnbaum, 2010; Brito-Zeron *et al.*, 2013), while central nervous system manifestations are less common. There are generally 3 neuropathy subtypes; large fibre, small fibre and ganglionopathy. Sensory ganglionopathy for example, may present as paraesthesia, unsteady gait and/or difficulties with fine motor movements due to decreased proprioception. Small fibre neuropathy may cause burning sensations, particularly in the feet and be more noticeable at night (Fauchais *et al.*, 2011; Berkowitz and Samuels, 2014).

1.3.16.2 Autonomic dysfunction

Autonomic dysfunction is common in PSS patients with a preponderance of certain symptoms such as orthostatic intolerance and vasomotor impairment (Cai *et al.*, 2008; Newton *et al.*, 2012; Ng *et al.*, 2012). Autonomic symptoms occur in over half of PSS patients and correlate with fatigue and depression (Newton *et al.*, 2012).

1.3.16.3 Cognitive impairment

Symptoms of cognitive impairment are significantly more apparent in a PSS population compared with controls and have been associated with cerebral frontal lobe white matter lesions (Segal *et al.*, 2010). The cognitive dysfunction and mild dementia seen in PSS patients is comparable with cognitive impairment seen in patients with multiple

sclerosis (Akasbi *et al.*, 2012; Blanc *et al.*, 2013). Furthermore, memory dysfunction in PSS has been associated with anti-NR2 antibodies in serum (Lauvsnes *et al.*, 2013).

1.3.17 PSS and mental health symptoms

PSS patients are significantly more likely to report symptoms of depression, with one study reporting an incidence of 47% in PSS patients compared with a 6% incidence in controls (Segal *et al.*, 2009). This incidence is higher than the rates of depression reported in other chronic diseases (9-23%) (Moussavi *et al.*, 2007). Depression is associated with reduced health related quality of life in PSS (Segal *et al.*, 2009; Lendrem *et al.*, 2014). In a recent study, depression in PSS was associated with raised anti-NR2 antibodies in cerebrospinal fluid and serum and this was the first study to demonstrate any potential relationship with depression in PSS and potential biomarkers (Lauvsnes *et al.*, 2013).

An increased level of psychological distress is reported in the PSS patients compared with healthy controls and certain personality features are more likely to be found in this patient group including perfectionism, negativity and preoccupation with detail (Price, 2016b). A recent Taiwanese population based retrospective cohort study found the adjusted hazard ratio of an anxiety disorder occurring in PSS patients was 1.86 (Shen *et al.*, 2015).

1.3.18 Fatigue

Fatigue is a dominant symptom for approximately 70% of PSS patients and is seen in 75% of patients with PSS (Ng and Bowman, 2010). Defined as '*an overwhelming sense of tiredness, lack of energy and a feeling of exhaustion*' (Shen *et al.*, 2006), it is a good predictor of poor health (Segal *et al.*, 2009) and is associated with functional impairment (Hackett *et al.*, 2012a; Fox and Fox, 2016). Previous studies have shown that physical fatigue measured with the somatic component of the Profile of Fatigue scale (Bowman *et al.*, 2004) is more prevalent and severe in PSS patients than mental fatigue as measured with the mental component of the same scale (Bowman *et al.*, 2004; Segal *et al.*, 2008; Theander *et al.*, 2010). Not surprisingly, PSS patients report excessive daytime sleepiness (Walker *et al.*, 2003; Theander *et al.*, 2010).

1.3.19 Sleep disturbances

Sleep is often disturbed in patients with PSS (Gudbjornsson *et al.*, 1993) and my recent systematic review found that a range of sleep disturbances are commonly reported in PSS patients including; subjective sleep disturbances, daytime sleepiness, night awakenings and obstructive sleep apnoea (Hackett *et al.*, 2016a). Sleep is further influenced by musculoskeletal pain and anxiety (Theander *et al.*, 2010) and sleep disturbance affects fatigue levels and can affect daytime functioning (Goodchild *et al.*, 2010).

1.3.20 Pain

Over half of PSS patients report chronic pain and 37-40% of patients in one study reported neuropathic pain, which was equally distributed amongst sero-positive patients (those with antibodies to Ro (SSA) or La (SSB)) and sero-negative patients (those with no SSA or SSB antibodies) (Segal *et al.*, 2013). Severe pain is reported more commonly in sero-negative patients (Segal *et al.* 2013). Pain in PSS is associated with functional difficulties (Hackett *et al.*, 2012a) and psychological distress (Segal *et al.*, 2014). Joint pain is a common feature of PSS affecting up to 54% of patients, and in some cases associated with clinically-apparent synovitis (Pease *et al.*, 1993).

1.3.21 Arthritis

Arthritis and/or arthralgia has been reported as being present in 54% of PSS patients (Pease *et al.*, 1993). Hand x-rays obtained from PSS patients revealed evidence of joint erosions in 33% of proximal interphalangeal joints, 27% of metacarpal phalangeal joints and 12% of wrist joints in PSS patients (Pease *et al.*, 1993).

1.3.22 Quality of life

Although mortality in PSS is similar to the general population, the disease has a profound impact on patients' quality of life (QOL) (Strombeck *et al.*, 2000; Meijer *et al.*, 2009; Ibn Yacoub *et al.*, 2012; Lendrem *et al.*, 2014). QOL is a broad concept, which attempts to describe general well-being of both individuals and societies (Carr *et al.* 1996) and incorporates function and mental and physical wellbeing. Studies have examined QOL in PSS using the Medical Outcomes Study Short Form-36 (SF-36) (Meijer *et al.*, 2009; Segal *et al.*, 2009; Cho *et al.*, 2013; Cornec *et al.*, 2017) and the European

quality of life – five dimension (EQ-5D) (Lendrem *et al.*, 2014). It seems that there are many co-dependant variables contributing towards QOL in PSS and large sample sizes and multivariate methods allow the variability in QOL in PSS to be broken down into component parts (Lendrem *et al.*, 2014). Only four studies have done this, and two with sample sizes >200. These include Lendrem *et al.*'s study (2014), which found pain and depression to be the greatest predictors of QOL measured by EQ-5D. Segal *et al.* (2009) however, found somatic fatigue was the dominant predictor of physical function and general health while depression was the main predictor of emotional well-being using the SF-36. Interestingly and perhaps rather alarmingly, data from the UKPSSR (Ng *et al.*, 2011) suggests that PSS patients are on average willing to sacrifice 3.7 months of their lives every year to be free from PSS (Lendrem *et al.*, 2014).

A recent study investigating predictors of poor QOL in PSS has confirmed that patient reported symptoms of pain, fatigue and dryness are greater predictors of reduced quality of life than systemic disease activity (Cornec *et al.*, 2017).

1.4 Measuring PSS disease activity and symptoms

1.4.1 Measuring symptoms and disease severity

A range of measures can be used to quantify various symptoms and disease severity in PSS. Disease severity scores, which show the systemic manifestations of the disease, are designed to be completed by a clinician. Symptom scores are usually patient-reported outcomes. The core set of measures which are collected in patients who have been recruited to the UKPSSR (Ng *et al.*, 2011) can be viewed in Table 1-2.

Clinician's assessment	Patient-reported outcome
AECG consensus criteria	Symptom assessment
Demographics	PROFAD
Treatment (pharmacological and non-pharmacological)	SSI
Comorbidity	ESSPRI
Disease activity	Epworth Sleepiness Scale
ESSDAI	Orthostatic Symptoms Scale
SCAI	Quality of life
SSDAI	EQ-5D
Disease damage	SF-36
SSDI	Anxiety and depressive symptoms
Optional	HADS
Cardiovascular risk assessment	Optional
	Autonomic symptoms and cardiovascular risk
	COMPASS
	Lifestyle (smoking, physical activity)

COMPASS: Composite Autonomic Symptom Scale; EQ-5D: European quality of life five dimensions; ESSDAI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index; ESSPRI: EULAR Patient Reported Index; HADS: Hospital Anxiety and Depression Scale; PROFAD: Profile of Fatigue and Discomfort; SCAI: Sjögren's systemic Clinical Activity Index; SF-36: Short Form 36; SSDI: Sjögren's Syndrome Damage Index; SSI: Sicca Symptoms Inventory.

Table 1-2 Core set of measures collected in patients recruited from the UKPSSR, adapted from Ng et al. (2011)

1.4.2 Composite scores

There are several different symptom and disease activity scores, which can be used in PSS. Consequently, an international group developed two consensus based activity indexes (Seror *et al.*, 2014). These indexes provide composite scores for PSS symptoms and disease activity:

- 1) Disease activity can be measured by the European League Against Rheumatism (EULAR) Sjögren's syndrome disease activity index – the ESSDAI (Seror *et al.*, 2010). The measure includes twelve organ specific domains, which are scored by a physician. The ESSDAI is sensitive to change and disease activity states can be scored as being low (ESSDAI <5), moderate ($\geq 5 \text{ESSDAI} \leq 13$) and high ($\text{ESSDAI} \geq 14$) (Seror *et al.*, 2016).
- 2) The EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) (Seror *et al.*, 2011) can be used as a composite symptom score and is completed by patients. It comprises of three 0-10 Likert rating scales for dryness, fatigue and pain. The composite score is the mean of the three domains. A disadvantage of the ESSPRI is that it is not as sensitive to change as the ESSDAI (Seror *et al.*, 2014). The patient satisfactory symptom state has been defined as ESSPRI <5 and the minimally important improvement as at least one point or 15% (Seror *et al.*, 2016).

Quality of life is measured using composite scores. As can be seen in Table 1-2, this can be evaluated in PSS using the EQ-5D (Brooks *et al.*, 2003) and the Short Form 36 (SF-36) (Ware and Sherbourne, 1992).

1.4.3 Objective dryness scores

Other objective measurements of disease activity include objective glandular function tests (Ng *et al.*, 2016). Schirmers I test measures tear production. A piece of filter paper is placed in the lower eyelid for 5 minutes. A measurement of ≤ 5 mm moisture indicates a positive test, whereas >10 mm of moisture shows normal tear production (Ng *et al.*, 2016). Other objective ocular assessments can include vital staining - where the eye is stained to assess damage; tear break-up time and tear film osmolarity (Ruaz, 2016).

Salivary gland function can be measured by testing salivary flow. Saliva is collected in a cup over five minutes and this can either be unstimulated, or stimulated with paraffin wax or citric acid (Vissink *et al.*, 2016). Ultrasound of the parotid gland and labial gland biopsy are alternative ways of examining the salivary glands (Vissink *et al.*, 2016).

1.4.4 Measuring symptom severity; patient reported measures

The main patient reported outcome measures which capture subjective symptoms scores from patients can also be seen in Table 1-2. In addition to these measures, the Ocular Surface Disease Index (Miller *et al.*, 2010) is a subjective measure of ocular symptoms, and 10cm visual analogue scales can be used to measure perceived global disease, pain, fatigue and dryness (Devauchelle-Pensec *et al.*, 2014).

1.5 Impact of PSS symptoms upon functional ability and participation

In this section, I first describe the World Health Organisation's (WHO) International Classification of Functioning, Disability and Health (ICF) model (WHO, 2001). I then summarise some pilot work, which forms the background to the studies contained within this thesis. This background work demonstrates the high levels of functional ability in PSS patients. I then describe how occupational therapists view function and participation, within the context of the ICF model and the Canadian Model of Occupational Performance (CMOP) (Townsend, 2002). Finally, I describe how the symptoms of PSS can affect specific areas of occupational performance.

1.5.1 The International Classification of Functioning, Disability and Health: Function and participation

The WHO describes the concept of functioning in the ICF model (see Figure 1:1). The ICF model is based on the biopsychosocial model of disability (Engel, 1977; Engel, 1980). In this model, a reduced ability to participate or function is due to a range of biological, psychological and social factors. The physiological functions of a person's body systems, their psychology and their involvement in life situations, can all influence the actions or tasks a person makes. Furthermore, all this needs to be considered within the context of environmental and personal factors (WHO, 2001). Consequently, disability can be regarded as a reduction in functional capacity in one or more domains of the ICF (Cieza *et al.*, 2014).

WHO describes participation as involvement in a life situation (WHO, 2001).

Participation is therefore about sharing or taking part, especially in activity and it is influential on health and well-being (Law, 2002). An example of participation is taking part in a sporting activity.

Functional ability may be different to participation, as a person may not be physically or cognitively able to complete an activity independently due to impairment. However, their impairment does not necessarily prevent them from participating, as appropriate support could enable participation e.g. a piece of equipment, or support from another person.

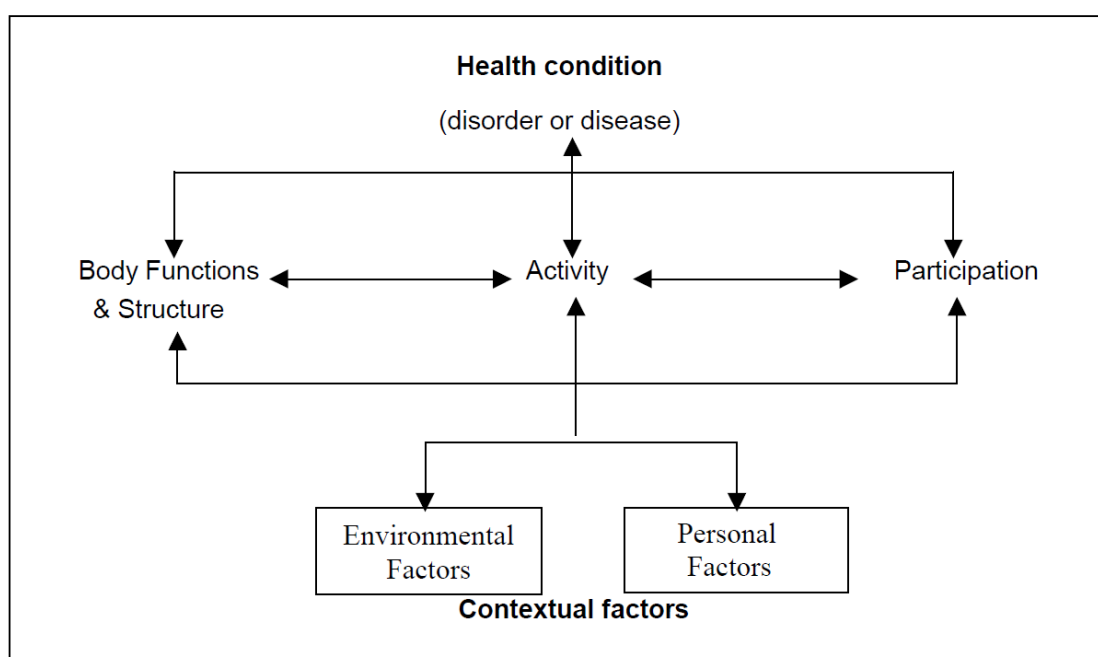


Figure 1:1 Conceptual framework of the International Classification of Functioning, Health and Disability (WHO 2002)

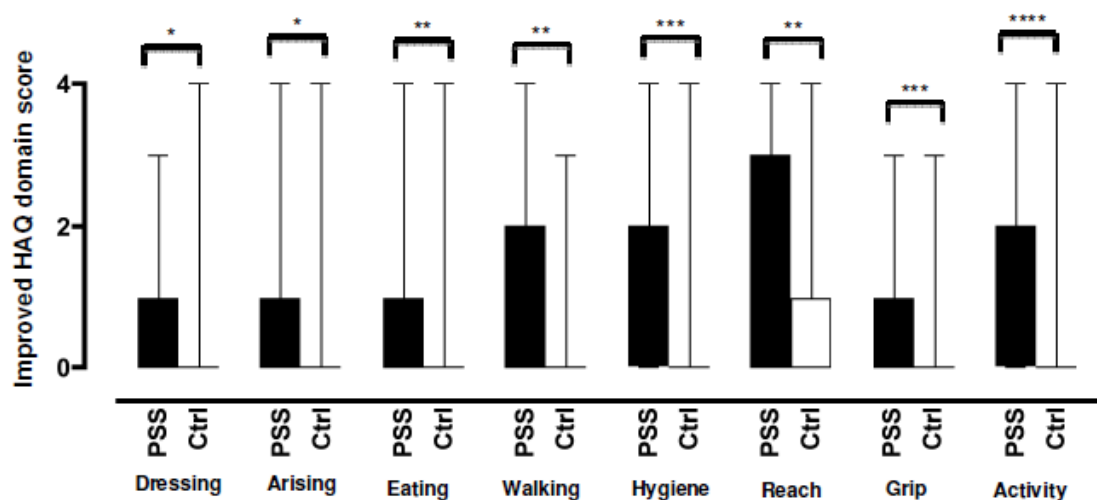
1.5.2 Functional difficulties in PSS

Recent studies in Newcastle have shown that liver-transplant recipients and patients with primary biliary cirrhosis or chronic fatigue syndrome (CFS) have significant impairment of their functional capacity which is independently associated with fatigue, orthostatic symptoms and daytime somnolence (Costigan *et al.*, 2010; Elliott *et al.*, 2011; Newton *et al.*, 2011). In PSS there are similar symptoms, however, the overall impact of these symptoms upon functional ability had not previously been reported. Therefore, prior to beginning my PhD work, I performed a study to systematically assess the physical function of patients with PSS using a validated instrument, the

Improved Health Assessment Questionnaire® (Improved HAQ) (Hackett et al., 2012a). The aim of the study was to assess the physical function of PSS patients and determine the relationship between the functional impairment experienced by PSS patients and disease activity, patient reported symptoms and quality of life. The following is taken from the published abstract.

Sixty nine PSS patients who fulfilled the AECG Classification Criteria completed the Improved HAQ. They also completed the following measures: European League Against Rheumatism (EULAR) Sjögren's Syndrome Patient Reported Index (ESSPRI), EULAR Sicca Scale (measures overall severity of dryness), Profile of Fatigue, Epworth Sleepiness Scale (measures daytime sleepiness), Hospital Anxiety and Depression Scale (measures anxiety and depression), Orthostatic grading Scale (measures orthostatic intolerance) and EuroQOL-5 domain (measures health related quality of life). In addition, the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and levels of systemic inflammation were assessed using C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Data were compared to 69 healthy volunteers matched for age and sex.

The study demonstrated that PSS patients experience greater functional impairment than controls (Improved HAQ total scores (mean±SD): PSS=24±25 vs. controls=9±19; $p=0.0002$) across all domains of activity. In PSS, functional impairment was significantly associated with physical fatigue ($p<0.0001$; $R^2=0.3$), pain ($p<0.0001$; $R^2=0.3$), depression ($p<0.0001$; $R^2=0.3$), total symptom burden ($p<0.0001$; $R^2=0.3$), systemic disease activity ($p=0.002$; $R^2=0.15$), quality of life ($p<0.0001$; $R^2=0.3$), dryness ($p=0.002$; $R^2=0.12$), daytime somnolence ($p=0.02$, $R^2=0.08$) anxiety score ($p=0.03$, $R^2=0.07$), and CRP ($p=0.04$, $R^2=0.06$). Only CRP was independently associated with functional impairment ($\beta=0.38$; $p=0.025$). (Hackett et al., 2012a).



* = $P < 0.05$; ** = $P < 0.01$; *** = $P < 0.001$; **** = $P < 0.0001$.

Figure 1:2 Individual Improved HAQ domain scores for PSS patients and controls (from Hackett et al., 2012a)

PSS patients experience significant functional disability compared to age-matched healthy controls. Impaired function was associated with reduced quality of life and symptoms such as pain, fatigue and depression as well as disease activity, illustrating the importance of optimal management of all aspects of the disease (Hackett *et al.*, 2012a).

1.5.3 Occupational therapy

Occupational therapists consider that participation in meaningful activities can have a positive influence on a person's health and wellbeing (Stamm *et al.*, 2006). A description of occupational therapy is given below:

Occupational therapy takes a whole-person approach to both mental and physical health and wellbeing, enabling individuals to achieve their full potential. Occupational therapy provides practical support to enable people to facilitate recovery and overcome any barriers that prevent them from doing the activities (occupations) that matter to them. This helps to increase people's independence and satisfaction in all aspects of life. (COT, 2016)

Occupational therapists therefore aim to enable people with health conditions to participate in, and carry out, functional activities of their choosing. In the context of the ICF model, they do this by addressing environmental and personal factors as well

as addressing body functions and structure. These activities or occupations can be grouped into self-care, productivity and leisure categories (ENOTHE, 2004).

In the following section, I describe the theoretical impact of PSS on self-care, productivity and leisure. This formed part of a publication, as well as the background work for my PhD research proposal (Hackett *et al.*, 2012b).

1.5.4 The impact of PSS on self-care, productivity and leisure

Symptoms and associated factors of PSS can influence the performance of those with the disease in their self-care, productivity and leisure activities. It was recently reported that PSS patients perceive that fatigue is the symptom which impacts most on their functional ability (Fox and Fox, 2016). However, a range of symptoms can also influence function and participation.

In this section, I provide an indication of how symptoms discussed earlier in this chapter (Section 1.3.10), may influence function and participation. I have used the domains of self-care, productivity and leisure, (which are described in the Canadian Model of Occupational Performance (CMOP) (Townsend, 2002) and the Canadian Occupational Performance Measure (COPM) (Law *et al.*, 2005a)), as a framework to structure the discussion.

1.5.4.1 PSS and self-care

The impact of having PSS can affect function and participation in a range of self-care activities.

I have already reported difficulties with aspects of personal care in this chapter (Section 1.5). Others have also reported difficulties with the self-care tasks of washing, dressing and toileting in this patient group (Sutcliffe *et al.*, 1998).

People with PSS can also have difficulty with eating due to severe xerostomia (dry mouth) leading to diminished taste, reduced appetite and difficulty in chewing and swallowing food (Palmer and Singh, 2008).

The consequences of dyspareunia and vaginal dryness in women with PSS can affect sexual function, pleasure and impact on personal relationships (Tristano, 2009; Maddali Bongi *et al.*, 2013). A further consequence of PSS symptoms within the context of personal relationships is oral dryness and the associated problems of a dry

mouth, including infections, lesions and halitosis as these can affect kissing (Tristano, 2009) and confidence at being within close proximity of others. Low mood, pain and fatigue are further symptoms, which can influence sexual functioning and personal relationships (Hackett *et al.*, 2012b).

Emotional expression, is also considered by the COPM as belonging within the self-care domain. This can affect people with PSS due to inflammation and damage to their lacrimal glands and hence an inability to make tears while crying (Hackett *et al.*, 2012b; van Leeuwen *et al.*, 2016).

Sleep is another factor, that lies within the self-care domain of the COPM. The sleep disturbance reported in people with PSS, including difficulties with falling asleep and more frequent and prolonged night waking (Gudbjornsson *et al.*, 1993) can have an impact on daytime physical and mental fatigue (Goodchild *et al.*, 2008). This in turn can affect many aspects of function and participation, including self-care activities.

In addition to the mobility difficulties previously described (in Section 1.5), another research group has shown that functional mobility can be affected due to a decrease in physical capacity which may be related to a person's experience of fatigue (Strombeck *et al.*, 2007). It also makes sense that the presence of muscle and joint pain in PSS patients, may also affect their mobility (Hackett *et al.*, 2012b). Therefore, individuals with PSS may experience difficulties with walking, manoeuvring in bed, managing stairs or transferring effectively (Hackett *et al.*, 2012a; Hackett *et al.*, 2012b).

Managing and organising tasks at home, work and within the community including budgeting, planning and driving may be affected by cognitive difficulties and mental fatigue (Goodchild *et al.*, 2010; Segal *et al.*, 2010; Hackett *et al.*, 2012b; Segal *et al.*, 2012; Blanc *et al.*, 2013). Fatigue, daytime sleepiness and pain could also have an impact on driving, and reduced clarity of vision due to dry eyes (Goto *et al.*, 2002) could further affect community management tasks such as driving, which demands a high degree of visual acuity.

1.5.4.2 PSS and productivity

Westhoff *et al* (2012) found that people with PSS who had higher levels of fatigue and depression were more likely to have increased levels of work disability. People with PSS are more likely to move to a less demanding schedule or job and less likely to

remain in employment (Meijer *et al.*, 2009; Bowman *et al.*, 2010). Oral dryness could be especially problematic in jobs relying heavily on oral communication such as teaching, call centre work or sales. Ocular dryness may particularly affect people whose jobs rely on visual clarity or prolonged use of visual display equipment, which in turn can exacerbate the symptom of dry eyes (Hackett *et al.*, 2012b). Furthermore, air conditioning systems and dry heat in the work place (which a person with PSS may have very little control over) can irritate the eyes (Ruaz, 2016).

Fatigue, pain, discomfort and impaired cognition can affect a person's ability and tolerance in carrying out domestic tasks such as food shopping, cooking, housework, cleaning and caring for children (Hackett *et al.*, 2012b). Bowman *et al.* (2010) have demonstrated that people with PSS have reduced capacity in carrying out household work.

Participation in education such as school, college or university may be affected by PSS. While it is rare for children to have this condition, it does affect some (Saad-Magalhaes *et al.*, 2011). It is more likely that adults may struggle to achieve their education goals due to physical and mental fatigue, pain, discomfort, difficulties with visual clarity and cognition. Furthermore, ocular dryness can result in difficulties with reading or using computer screens for periods of time and oral dryness may mean that giving verbal presentations can be problematic.

1.5.4.3 PSS and leisure activities

Capacity to undertake quiet recreational tasks such as reading or crafts might be reduced, due to reduced concentration and cognition. Ocular dryness can make reading, using a computer and watching films or television more uncomfortable and tiring (Hackett *et al.*, 2012b).

Active recreation, including participation in sports is likely to be affected due to decreased physical capacity and reduced aerobic capacity (Strombeck *et al.*, 2007). Fatigue and pain may also be limiting factors in taking part in active recreation.

Sutcliffe *et al.* (Sutcliffe *et al.*, 1998) have shown that a proportion of people suffering from PSS are restricted in their social activities such as visiting friends. People with the condition often report that they do not have enough energy to go out socially because of fatigue. Due to their dry mouth and difficulties in swallowing, many individuals with

PSS also avoid dining out because of their concern about the kind of food that they can eat as well as causing potential embarrassment from taking excessive time in consuming the food (Hackett *et al.*, 2012a).

A further consequence of how oral dryness may result in further social isolation is evident from the following statement:

I rarely smile or talk in public since my inability to produce saliva has caused embarrassing tooth decay. (Sjögren's Syndrome Foundation, 2016)

The consequences of oral dryness mean that this person has now changed how they relate to others in social situations.

1.5.5 Developing interventions for PSS

I have demonstrated from the literature that there are a range of symptoms in PSS, which seem to influence participation and the ability to perform daily activities. It therefore seems appropriate to develop some form of intervention to support and enable PSS patients to do the activities in life they want to or need to do. Such an intervention is likely to be complex, as it will comprise of '*various interconnecting parts*' which are likely to have more variation than a drug (Campbell *et al.*, 2000).

1.5.5.1 Developing complex interventions: The MRC Framework

The Medical Research Council (MRC) framework for complex intervention development (Craig *et al.*, 2008) recommends an iterative stepped, structured, mixed-methods approach to designing and developing a complex intervention. This pathway can be compared to that which is followed in the development of a new drug (Campbell *et al.*, 2000) (see Figure 1:3).

Figure taken from (Campbell et al., 2000) and (Thornicroft et al., 2002).

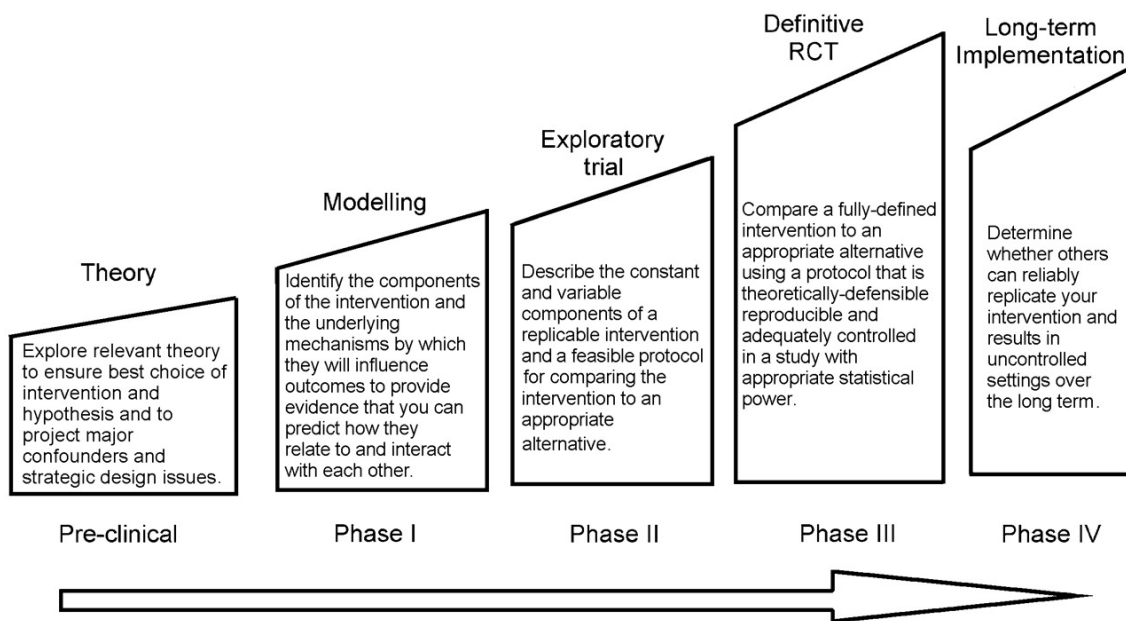


Figure 1:3 Sequential phases of developing randomised controlled trials of complex interventions (Campbell et al. 2000)

However, although the MRC framework for complex intervention development has been developed, there is an acknowledgement that the development of a complex intervention does not always follow a linear process. Therefore the development of a complex intervention may start in the development phase, then move into the feasibility and piloting stage, be followed by a formal evaluation of effectiveness and finally move into the implementation phase (Craig *et al.*, 2006) (see Figure 1:4). This process may involve several backward steps along the way. For example if the developed intervention is not deemed as being feasible during the feasibility and piloting phase.

Figure taken from (Craig et al., 2006)

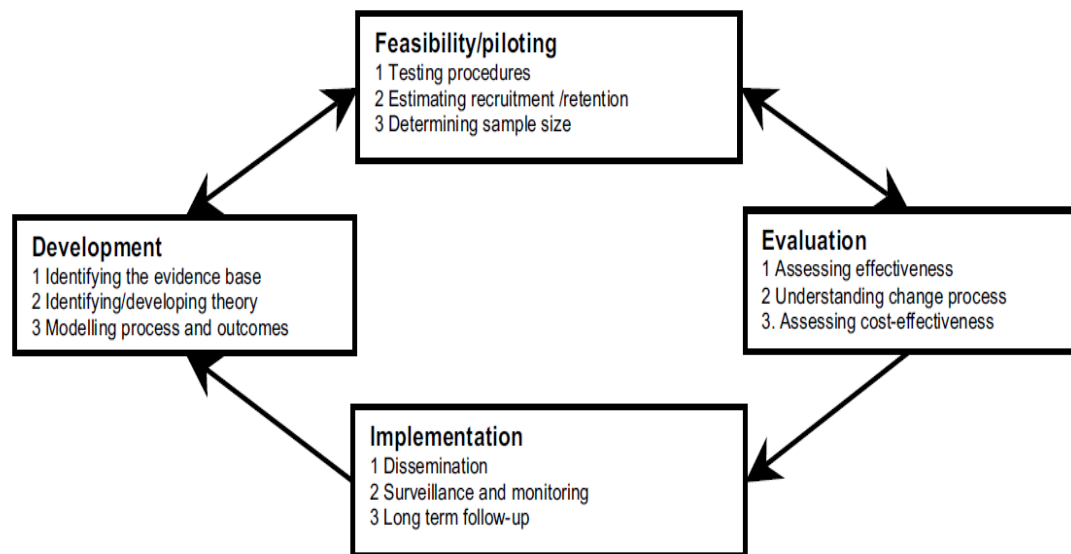


Figure 1:4 The MRC Framework: Key elements of the development and evaluation process (Craig 2006)

In the development stage, when little is known about the bio-psychosocial determinates of illness and illness-associated functional capacity, a combination of qualitative techniques to explore and describe patient experience and review of the existing evidence is recommended. Such findings will then form the theoretical and empirical basis for intervention development, and disease model construction. The key tasks of this stage are to identify intervention targets, the mechanisms whereby the proposed intervention will lead to functional change, and a specification of how this change will be measured.

1.6 Aim and objectives

The aim of this PhD study is to develop a model for intervention in PSS (Hackett *et al.*, 2014).

The objectives are:

1. To determine the effectiveness of any current non-pharmacological interventions for PSS.
2. To collect data from different stakeholder groups to identify priority intervention target areas in PSS.
3. To use existing clinical evidence to establish the optimum intervention targets and mechanism of effect of intervention for selected intervention targets.
4. To establish which of these priority areas could realistically be delivered within a UK NHS setting.

1.7 Summary structure of the thesis

The studies contained within this thesis fall within the development stage of the MRC complex intervention framework (Craig *et al.*, 2006). In Chapter 2, I present a summary of existing evidence of non-pharmacological interventions for PSS. In Chapter 3, I present a mixed methods concept mapping study in which candidate intervention targets are identified and prioritised by patient, family and health care professional stakeholders. I explore the results of this study further in Chapter 4 with input from clinicians. In Chapters 5, 6 and 7, I explore the priority targets and delivery of possible future interventions with patient and family member stakeholders in qualitative focus group discussions. I present the overall conclusions in Chapter 8, together with recommendations for future research.

Chapter 2. A systematic review of non-pharmacological interventions for primary Sjögren's syndrome

In Chapter 1, I demonstrated the impact the symptoms of PSS can have on those with the disease, in particular, how these symptoms may affect patients' ability to participate fully in daily life by engaging in activities of their choosing or by taking on life roles. The conclusion of Chapter 1 was that, although non-pharmacological interventions may improve participation and increase function ability, we do not know which interventions, if any, work. Furthermore, the effectiveness of non-pharmacological interventions for this patient group are not yet known. In this chapter, I report the methods and results of a systematic review where I have searched for all the available published evidence of non-pharmacological interventions for PSS and assessed their effects.

2.1 Background and rationale for this systematic review

Non-pharmacological interventions for PSS may vary according to the particular symptom, which they are targeting. They may be complex, target several symptoms at once and be conducted by more than one member of a multidisciplinary team (Guillemin *et al.*, 2011). Such interventions may include fatigue and mood management (Westhoff *et al.*, 2012) and patient education by healthcare professionals (Cockshott *et al.*, 2005). Other interventions may be conducted by a clinician with specialist skills; such as occupational therapy to establish a balance in daily activities and improve function (Hackett *et al.*, 2012b); insertion of lacrimal punctal plugs for dry eye symptoms (Valim *et al.*, 2015) or the use of acupuncture for the symptomatic relief of dry mouth (O'Sullivan and Higginson, 2010).

Treatments in clinics for people with PSS tend to focus on pharmacological interventions. However, a recent systematic review has shown that evidence to support efficacy of pharmacological therapies in PSS is poor (Ramos-Casals *et al.*, 2010). Given the range of bio-psychosocial symptoms that these patients experience, it is possible that there are effective non-pharmacological treatments which could improve symptoms. The reduced impact of symptoms consequently may lead to an

improvement in quality of life, improved work capacity and a reduction in economic costs to society.

2.1.1 Aims

The aims of this review were to identify published randomised controlled trials (RCTs) of any non-pharmacological interventions for adults with PSS and to assess the effects of these interventions on any outcome on these patients.

2.2 Methodology

2.2.1 Justification of methodology

A general review of the literature on any topic can highlight key papers in the area of interest. However literature reviews which are not systematic are inherently subject to greater levels of bias compared with a systematic approach following explicit methods (Mulrow, 1994). A systematic literature review provides an effective approach to integrate existing information, provide data for decision making, to establish whether findings are consistent between studies and determine whether they can be generalised across populations and settings. Furthermore using explicit methods (particularly when registered a priori) limits bias and should improve reliability and accuracy of conclusions, compared with non-systematic approaches (Mulrow, 1994). A systematic approach was therefore taken to conduct this sub-project and the protocol was registered a priori in the PROSPERO database (Hackett *et al.*, 2013).

2.2.2 The systematic review process

2.3 Method

I identified relevant experimental studies and based my methods on those recommended in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2008).

2.3.1 Types of studies

All RCTs were included in this review. Non-randomised studies were excluded as potential biases are likely to be greater in these studies compared with RCTs (Reeves *et al.*, 2008). Selection bias can be a particular problem in non-randomised studies.

Biased selection of participants can occur in both RCTs and non-randomised studies. However, biased allocation to an intervention group can be a particular problem in non-randomised studies, when participants selected for an intervention have differing characteristics from those who are allocated to a control group or alternative intervention. A clinician often has this choice, but it can also be influenced by patient preference or a patients' disease severity. This bias can result in unmatched groups such as the intervention group containing a greater proportion of participants with severe illness compared with the alternative group (Bradford Hill, 1977; Deeks *et al.*, 2003; Reeves *et al.*, 2008). Therefore, only RCTs were included in this review.

2.3.2 Types of participants

I included adult participants (over the age of 18) with a diagnosis of PSS. Children rarely develop PSS and, as I was looking to develop interventions for adults with PSS, it was logical to only include adults in the systematic review. Although it would be useful to only include studies which have used the American European Consensus Criteria (AECG) for PSS (Vitali *et al.*, 2002), I included all PSS patients diagnosed by a clinician. I did not stipulate the use of these criteria as I anticipated that there would be very few studies left to be included the review. However the criteria for diagnosis is discussed in the results.

2.3.3 Types of interventions

I considered all non-pharmacological interventions which aimed to improve a symptom or symptoms of PSS were for inclusion. Pharmacological interventions are classified as medicinal products in accordance with EU Directive 2001/83/EEC (Council Directive, 2001) and these were excluded from the review. I regarded homeopathic remedies, herbal medicines and trials of vitamins as pharmacological interventions for the purpose of this review and these were excluded, as the claimed mechanism of action is a chemistry change within the body. I also excluded surgical procedures. The comparison could be a placebo, alternative intervention which may be pharmacological or non-pharmacological, or usual care.

2.3.4 Types of outcome measures

The outcomes I considered within this review fell within the main domains addressed by the World Health Organisation (WHO) International Classification of Functioning Disability and Health (ICF)(WHO, 2001) (see Figure 1:1).

2.3.4.1 Primary Outcomes

Primary outcomes included assessments of activities of daily living, for example, the short-form (SF)-36 physical functioning scale (Ware and Sherbourne, 1992) and the improved HAQ (Fries *et al.*, 2009); and participation outcomes pertaining to work, return to work and social engagement, measured by, for example, The Work and Social Adjustment Scale (Mundt *et al.*, 2002).

2.3.4.2 Secondary Outcomes

Impairment of body functions and structures included outcomes of mood, dryness, disease activity, daytime sleepiness, fatigue and cognitive function. Environmental factors included outcomes of costs, carer strain and willingness of employer to adapt the work environment. Personal factors included self-efficacy level of education and quality of life. Adverse events were also considered.

2.3.5 Search methods for identification of studies

There are a large number of possible non-pharmacological interventions and each may have many synonyms. I therefore performed a search for any randomised controlled trial or controlled clinical trial for PSS initially. I combined the Medical Sub Headings (MeSH) terms and keywords for PSS with the Cochrane Highly Sensitive Search Strategy for identifying randomised controlled trials (Lefebvre, 2008). The Medline search terms can be viewed in Table 2-1.

Search Terms	
sjogrens syndrome/	randomly.ab.
sjogrens syndrome.mp.	trial.ab.
1 or 2	groups.ab.
randomized controlled trial.pt.	4 or 5 or 6 or 7 or 8 or 9 or 10
controlled clinical trial.pt.	exp animals/ not humans.sh.
randomized.ab.	11 not 12
placebo.ab.	3 and 13

Table 2-1 Medline search terms

I carried out electronic searches on the following electronic databases from inception to June 2016: Cochrane Central Register of Controlled Trials (CENTRAL); Cochrane Database of Systematic Reviews (CDSR); Medline via OVID; Embase via OVID; PsychINFO via OVID; Cinahl via EBSCO; Current Controlled Trials Register (USA); World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP); The National Research Register Archive (NRR) (UK); The UK Clinical Trials Gateway (UK).

I imported the titles and abstracts into Endnote Version X7 reference managing software, combined them into one file, removed duplicate titles and reviewed the titles and abstracts of all remaining studies.

2.3.6 Selection of studies

I reviewed titles and abstracts of all remaining studies and highlighted all studies which initially seemed to fit the inclusion criteria. A second reviewer (Victoria Strassheim) also carried out this screening process independently to ensure that no relevant studies were missed (Edwards *et al.*, 2002). I obtained full text articles for all highlighted studies.

Next, I screened all full text articles against the inclusion criteria. This process was also carried out independently by a second reviewer (Katherine Deane). The purpose of having two reviewers was again, to minimise bias. Some experts suggest that it can be advantageous having a second reviewer who is not an expert in the subject area of the systematic review (Higgins and Deeks, 2008) as this can help reduce bias. We resolved

any disagreements over decisions through discussion. I then searched the reference list of studies fitting the inclusion criteria for any further potential studies for inclusion and retrieved the full text articles of any titles seeming to fit the criteria. These were reviewed both by myself and the second reviewer (KD).

2.3.7 Assessment of risk of bias

I reviewed the studies for methodological quality using the Cochrane Risk of Bias Tool (Higgins and Altman, 2008). This process was repeated independently by a second reviewer (KD) and again, any discrepancies were easily resolved through discussion. Six items were used to assess risk of bias using only published material. I contacted the authors to seek clarification, but no replies were received so a number of items remained unclear.

The following types of bias were assessed and follow the materials which accompany the Cochrane Risk of Bias Tool (Higgins and Altman, 2008):

- i. *Random sequence generation*: The methods used to determine which group a participant would be randomised to, were assessed. Random sequence generation usually results in prognostic factors being balanced evenly between groups. Methods which were not considered to be random, such as alternation (where consecutive participants are randomised to alternate groups) were considered to be at high risk of bias, as the future assignment of a participant might be anticipated which could result in selective enrolment in light of the predicted group allocation.
- ii. *Allocation concealment (selection bias)*: The method used to conceal the allocation sequence was assessed. A study was deemed to be of high risk of bias if the investigators enrolling participants and the participants could foresee which group a participant might be allocated to. Methods such as central allocation (e.g. telephone or web-based randomisation) can be used to conceal allocation and minimise selection bias.
- iii. *Blinding of participants and personnel (performance bias)*: A study was deemed to be at high risk of performance bias if participants or study personnel had knowledge of which group the participant was allocated during the study.
- iv. *Blinding of outcome assessment (detection bias)*: If the outcome assessors had knowledge of participants' group allocation, the study was deemed to be at high risk of detection bias.
- v. *Incomplete outcome data (attrition bias)*: If incomplete outcome data were not addressed adequately, the study was deemed to be at high risk of attrition bias.
- vi. *Selective reporting (reporting bias)*: A study was deemed to be at low risk of reporting bias if the authors had published an a priori protocol and the pre-specified primary and secondary outcomes were reported as indicated in the protocol. If there was no protocol available, the study was scored as unclear risk of reporting bias as it is impossible to tell whether the outcomes reported were those which were originally planned prior to the start of the study.
- vii. In addition to scoring each of the above items, for risk of bias, an overall risk of bias score was awarded to each included study. I scored each study (with agreement from the second reviewer KD) as being at:
 - *Low risk of bias* if ≥ 4 of the individual items were deemed to be at low risk of bias.

- *Moderate risk of bias* if 1-3 individual items were deemed to be at low risk of bias and a maximum of 2 individual items were deemed to be at high risk of bias.
- *High risk of bias* if no individual items were deemed to be at low risk of bias and/or >2 individual items deemed to be at high risk of bias.

2.4 Results

2.4.1 Search Results

The literature search, including the ten databases resulted in the identification of 1806 records. 174 duplicate papers were removed. A hand search of the references from the included papers revealed a further 2 studies.

2.4.2 The Selection of Papers for Inclusion

Following a review of the potential relevance of all 1814 citations, 149 titles were duplicates. Following a review of titles and abstracts of the remaining 1657 titles, the full texts of 20 studies seemed to match the inclusion criteria and were retrieved. After reading the full texts of these 20 studies, 12 studies were deemed not to fit the inclusion criteria. The remaining 8 studies were included in the review. The references of these included papers were checked and a further 2 full text papers were retrieved. However, after reviewing the full texts, these papers were deemed by both reviewers (KH and KD) not to fit the inclusion criteria. This left a total of 8 papers which for inclusion in the systematic review. Due to the heterogeneity of the included studies, no papers were included in a meta-analysis. Figure 2:1 is a PRISMA flow diagram (Moher *et al.*, 2009) demonstrating the steps taken during the selection of papers for inclusion in this review. Table 2-2 reveals the numbers of records identified within each database.

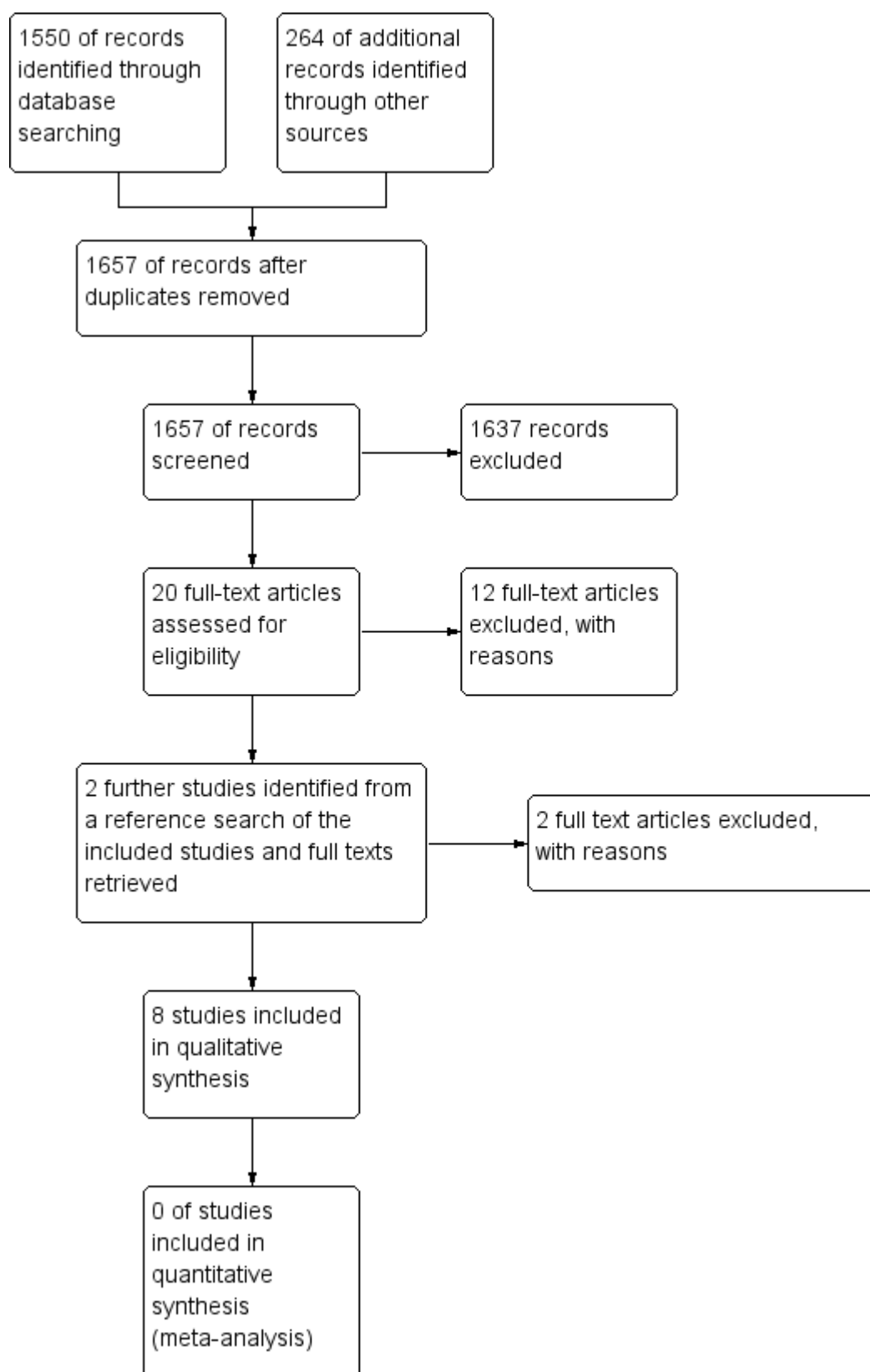


Figure 2:1 PRISMA Flow diagram of study selection

Database	Number of Records
AMED	8
CENTRAL	62
CDSR	3
CINAHL	177
Current Controlled Trials Register	62
Embase	52
Medline	1136
National Research Register Archive	70
PsychINFO	177
UK Clinical Trials Gateway	2
WHO ICTRP	65

Table 2-2 Results of the systematic review search of ten databases

2.4.3 Excluded studies

The 14 publications which were subsequently excluded did not meet the review inclusion criteria: 8 were not RCTs (Freeman, 1975; Blom *et al.*, 1993; Frost *et al.*, 1997; Blom and Lundeborg, 2000; Strombeck *et al.*, 2000; Bai *et al.*, 2007; Strombeck and Jacobsson, 2007b; Strombeck *et al.*, 2007), 4 did not report the PSS data separately for PSS participants (Steller *et al.*, 1988; Talal *et al.*, 1992; Frost *et al.*, 2002; Strietzel *et al.*, 2011) and 2 studies were conference abstracts only (Migita *et al.*, 1982; Ngo *et al.*, 2015) (see Table 2-3).

Study	Reason for Exclusion
Bai (2007)	Not an RCT
Blom (1993)	Not an RCT
Blom (2000)	Not an RCT
Freeman (1975)	Not an RCT
Frost (1997)	Not an RCT
Frost (2002)	PSS data not reported separately for PSS patients
Migita (1982)	Abstract only, outcomes not reported
Ngo (2015)	Abstract only
Steller (1988)	PSS data not reported separately for PSS patients
Streitzel (2011)	PSS data not reported separately for PSS patients
Strombeck (2000)	Not an RCT
Strombeck (2007a)	Not an RCT
Strombeck (2007c)	Not an RCT
Talal (1992)	PSS data not reported separately for PSS patients

Table 2-3 Excluded studies with reasons for exclusion

There were 2 registered relevant clinical trials identified which have yet to publish data. These trials are either in process or have not yet published their findings in full (see Table 2-4).

Ongoing clinical trials
Effects of exercise training in PSS, myositis and Takayasu's arteritis: University of Sao Paulo, Brazil (Miyamoto, 2015)
Effect of debridement-scaling on the relief of dry eye signs and symptoms in Sjogren's syndrome: University of Waterloo, Ontario, Canada (University of Waterloo, 2014)
Management of fatigue in sicca syndromes: University of Utrecht, Netherlands (van Leeuwen, 2012)

Table 2-4 Ongoing clinical trials

2.4.4 Included studies

The final selection, based on consensus resulted in 8 trials being included in the review (Poulsen, 1991; List *et al.*, 1998; Frost *et al.*, 2006; Mansour *et al.*, 2007; Qiu *et al.*, 2013; Cafaro *et al.*, 2015; Li *et al.*, 2015; Lin *et al.*, 2015). See Table 2-5 for a description of the included studies.

Study	Description of Intervention	Comparator	Participants	Quality	Results
Cafaro 2015	Laser acupuncture to increase salivary flow	Placebo laser acupuncture (no radiation was emitted)	n=26 Female=26 Average age=70	Low risk of bias	Improvement in salivary flow
Frost 2006	Intra oral lubricating device	Treatment as usual	n=29 Female=27 Average age=62	Moderate risk of bias	Whole saliva and 'PUTTICA' speech test improved. No difference in dryness outcome
Li 2015	Silicone hydrogel contact lenses	Autologous serum eye drops	n=37 Female=36 Average age=48	Moderate risk of bias	Improvement in corneal staining
Lin 2015	Acupuncture for dry eyes	Carboxymethyl-cellulose sodium eye drops	n=18 Female=6 in intervention group and 0 in control group	Moderate risk of bias	No difference between groups

List 1998	Acupuncture to increase salivary flow	Treatment as usual (waiting list)	N=21 Female=20 Average age=65	Moderate risk of bias	Saliva production not stated. Mouth and eye burning not stated. No difference between groups
Mansour 2007	Punctum plugs for dry eyes	Treatment as usual	n=20 Female=17 Average age=55	High risk of bias	No data extractable from the full text paper. Results unknown.
Poulson 1991	Psychodynamic therapy	Treatment as usual (waiting list)	N=18 Female=16 Average age=54	High risk of bias	No difference between groups
Qui 2013	Punctum plugs for dry eyes	Eye drops	n=42 Female=36 Average age=35	Low risk of bias	No difference between groups. Each group improved.

Table 2-5 Description of the included Studies

2.4.5 Risk of bias in included studies

See Figure 2:2 for a risk of bias summary, which demonstrates the reviewer's judgements about each risk of bias item for each included study. Each risk of bias item within the figure is discussed in turn.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cafaro 2015	+	+	?	?	+	?	+
Frost 2006	?	?	-	?	?	?	+
Li 2015	?	?	-	?	-	?	+
Lin 2015	?	?	-	-	?	?	+
List 1998	?	?	-	?	-	?	+
Mansour 2007	+	?	-	-	-	?	+
Poulsen 1991	?	?	-	-	-	-	-
Qiu 2013	+	+	-	+	-	?	+




 High risk of bias
 Low risk of bias
 Unknown risk of bias

Figure 2:2 Risk of bias summary: reviewers' judgements about each risk of bias item for each included study

Sequence generation was judged to be at low risk of bias for three studies (Mansour *et al.*, 2007; Qiu *et al.*, 2013; Cafaro *et al.*, 2015). Two used computer generated randomisation schemes (Mansour *et al.*, 2007; Qiu *et al.*, 2013) and two other studies a permuted random block approach (Cafaro *et al.*, 2015; Lin *et al.*, 2015). However Lin *et al.* (2015) did not fully explain their randomisation methods in the text. The method

of sequence generation was not discussed within the text of the remaining four included studies (Poulsen, 1991; List *et al.*, 1998; Frost *et al.*, 2006; Li *et al.*, 2015) and was therefore deemed to be of unclear risk of bias. Concealment of allocation was judged to be at low risk in only two studies (Qiu *et al.*, 2013; Cafaro *et al.*, 2015). In one study (Cafaro *et al.*, 2015) the sealed envelopes were opened at the first laser acupuncture session and in the other (Qiu *et al.*, 2013), random allocations were placed in sealed opaque envelopes marked with study identification numbers by the same clinical staff. The remaining six studies did not include a discussion of allocation concealment and were judged to be of unknown risk of bias.

Blinding was not conducted in any of the studies except one (Cafaro *et al.*, 2015). In this study the participants did not know if they received the active laser acupuncture. The same equipment was used for both groups, with the same noise but the control group did not receive the radiation. In all remaining studies, the participants were not blinded as to the arm of the study they were in and this lack of blinding was judged to make these studies to be at high risk of bias. However blinding the participants to the interventions would be difficult with many of the included non-pharmacological interventions. Detection bias was deemed to be low in one study (Qiu *et al.*, 2013) where the staff performing the assessments and analyses were blinded to the treatment allocation. Three studies were judged to be at high risk of detection bias as the outcome assessors were not blinded (Poulsen, 1991; Mansour *et al.*, 2007; Lin *et al.*, 2015) and the remaining four studies did not mention whether outcome assessors were blinded to treatment allocation, so the risk of bias was unclear.

Five out of the eight included studies were at high risk of bias from incomplete outcome data. Follow up measurements were not taken for all of the participants who took part in one study and their baseline data were not presented in the analysis (Poulsen, 1991). In a study on punctum plugs, six participants had spontaneous plug loss and a further participant suffered from a reaction to the plug and the data from these seven participants were excluded from the analysis (Mansour *et al.*, 2007). Two participants were lost to follow up in two separate studies and their data were excluded from the analyses (List *et al.*, 1998; Qiu *et al.*, 2013). In the study by Li *et al.* (2015), baseline data were reported for all participants who were recruited to the study. However, the data of three participants who withdrew from the study were not

imputed and included in the analysis. The authors did include data in the final analysis from three further participants who did not attend their final follow-up visit. In one study (Frost *et al.*, 2006) the data presentation was unclear and it was not possible to determine if the analysis was intention to treat. Another study only included the demographic data for those who completed the study (Lin *et al.*, 2015) and it is not possible to tell whether the PSS patients were amongst those who withdrew from the study. In the remaining study (Cafaro *et al.*, 2015), all participants completed the study and their data were included in the analysis.

I did not have access to the study protocols and was unable to assess the selective reporting risk and have reported this parameter as 'unclear' in seven of the studies (List *et al.*, 1998; Frost *et al.*, 2006; Mansour *et al.*, 2007; Qiu *et al.*, 2013; Cafaro *et al.*, 2015; Li *et al.*, 2015; Lin *et al.*, 2015). One study was judged to be at high risk of selective reporting (Poulsen, 1991) as an alexithymia (difficulty in identifying and describing emotions) measurement was only taken after treatment in the experimental group and was compared with baseline measurements from the control group in the analysis.

2.4.6 Participants

Overall 211 participants with PSS were included in these 8 studies. The number of participants with PSS in these studies ranged from 42 (Qiu *et al.*, 2013) to 18 (Poulsen, 1991; Cafaro *et al.*, 2015). All studies recruited both males and females except one which recruited females only (Cafaro *et al.*, 2015). The numbers of males recruited to each remaining study were low and ranged from 1 (List *et al.*, 1998; Li *et al.*, 2015) to 4 (Qiu *et al.*, 2013). The gender distribution of the study population however, is representative of the PSS population (Qin *et al.*, 2015).

A range of diagnostic criteria were used in the included studies. One study (List *et al.*, 1998) included participants diagnosed with PSS according to the Copenhagen (Manthorpe *et al.*, 1986), the San Diego Criteria (Fox and Saito, 1994) and the proposed European Community Study Group Criteria (Vitali *et al.*, 1996). Four studies (Qiu *et al.*, 2013; Cafaro *et al.*, 2015; Li *et al.*, 2015; Lin *et al.*, 2015) reported that participants were diagnosed according to the AECG criteria (Vitali *et al.*, 2002). Mansour *et al.* (Mansour *et al.*, 2007) recruited participants diagnosed according to the

European Criteria (Vitali *et al.*, 1996). The remaining studies (Poulsen, 1991; Frost *et al.*, 2006) did not specify how the participants were diagnosed, although Frost *et al.* (Frost *et al.*, 2006) did specify they recruited their participants from a Sjögren's syndrome clinic. (See Table 2-6 for a summary of the main findings of the 8 selected studies).

Studies included in the review: Summary of main findings	
Cafero et al 2015	
Methods	Single blind, randomised controlled trial.
Participants	26 women with a diagnosis of PSS made by a specialist using the AECG criteria. Average age 69 years.
Interventions	Laser acupuncture to increase salivary flow rate. This was delivered weekly over 5 sessions. Specific acupuncture points were stimulated bilaterally with an irradiation time of 120 seconds per acupoint. The control group received a placebo; the same equipment was used, with the same sound, but no radiation was emitted.
Outcomes	Oral Schirmer's test - unstimulated salivary flow rate (mm/5 minutes).
Frost et al 2006	
Methods	Single blind, randomised cross over study.
Participants	29 patients from a Sjögren's syndrome clinic. 27 female. Average age 62 years.
Interventions	Oral lubrication device containing a saliva substitute gel versus lubrication with their preferred method (sips of water, saliva substitute gel, sugar free chewing gum). The oral device was fitted for one week.
Outcomes	Oral lubrication diary; questionnaire regarding ability to speak, chew and swallow; a clinician reported dry mouth score (1-13 scale); a whole mouth unstimulated salivary flow (10 minutes); bacteriological sample; a parotid stimulated flow (10 minutes); a speech test (the phoneme sequence 'PUTTICA' was repeated as many times as possible over a 2 minute period); periodontal measurements (pocket depth, plaque and bleeding).
Li et al 2015	
Methods	Parallel randomised unblinded controlled study.
Participants	37 participants with PSS and dry eye attending an eye hospital. 36 female. Average age 48 years.
Interventions	Silicone hydrogel contact lenses worn continuously for 6 weeks. These were replaced after 3 weeks with new lenses if there were any signs of wear or problems with lens fit. The control arm received autologous serum eye drops. They were asked to use the drops 8 times a day for 6 weeks.
Outcomes	Visual acuity, corneal fluorescein staining, slit-lamp biomicroscopy to examine the anterior segment, tear production (Schirmer test), tear break up time. Measurements were recorded at baseline, week 3, week 6 and 6 weeks after therapy was withdrawn.

Lin et al 2015	
Methods	Parallel randomised unblinded controlled study.
Participants	18 patients with PSS diagnosed according to the AECG criteria. All female in control group and male-to-female ratio in intervention group reported as 0.29. Average age of 47.
Interventions	All participants undertook 2 weeks' washout where all treatments for dry eye were stopped. The intervention group then received 12 acupuncture sessions, 3 times a week over 4 weeks. The control group received carboxymethylcellulose sodium eye drops four times a day for 4 weeks in both eyes.
Outcomes	Subjective symptom assessment of visual function, bothersome symptoms and environmental triggers. Imaging of tear meniscus using optical coherence tomography (height, depth and tear meniscus area). Tear break up time. Schirmer test.
List et al 1998	
Methods	Parallel randomised unblinded controlled study.
Participants	21 patients with primary Sjögren's syndrome diagnosed according to the Copenhagen and San Diego criteria, 20 female and an average age of 65.
Interventions	Acupuncture twice a week for 10 weeks. Each treatment was 30 minutes. The needles were placed intramuscularly, mainly in the regions of the parotid submandibular and labial glands. The needles were stimulated manually and electrically (see paper for details). The control arm received treatment as usual which was not specified.
Outcomes	Patient reported degree of discomfort from mouth dryness, eye dryness and tongue and mouth burning (10 point VAS). Patient reported reduction in speech and chewing and a separate question on ADL (both 10 point VAS). The overall subjective experience of the treatment effect (6 point scale). Unstimulated salivary secretion rate (mL/15 minutes) and paraffin stimulated saliva secretion rated (mL/5 minutes).
Mansour et al 2007	
Methods	A parallel unblinded randomised controlled study. NB The patients' eyes were randomised to the intervention or control group.
Participants	20 patients with dry eyes caused by Sjögren's syndrome, diagnosed according to the European criteria. 17 women and an average age of 55 years.
Interventions	Uni-ocular punctum occlusion versus no treatment in the other eye.

Outcomes	The Schirmer test, rose Bengal staining, mucus debris in the cul-de-sac of both eyes, subjective discomfort of patients.
Poulson 1991	
Methods	A parallel randomised controlled study
Participants	18 PSS patients. Diagnostic criteria not specified. 16 Female and average age of 54 years.
Interventions	Group psychotherapy of 12 meetings of 1.5 hours each, twice a month over 6 months. The control group were assigned to a waiting list and offered the intervention at the end of the study.
Outcomes	Toronto Alexithymia scale, self-report questionnaire about benefit, Yalom's curative factor Q-sort, semi-structured clinical assessment interview.
Qui et al 2013	
Methods	Parallel group randomised controlled trial with blinded outcome assessors
Participants	42 participants with dry eyes diagnosed with PSS according to the AECG Criteria. 36 female and an average age of 35.
Interventions	A thermo sensitive punctal plug versus artificial tear solution containing a carbomer gel and basic fibroblast growth factor. Patients in the artificial tears group used the artificial tear solution 4 times a day with one drop instilled each time into the inferior conjunctival sac of both eyes. Patients in the plug group underwent punctal plug insertion in both the superior and inferior lacrimal puncta.
Outcomes	Ocular Surface Disease Index; corneal fluorescein staining; tear film break up time; Schirmer I test; contrast sensitivity and glare disability.

ADL: Activities of daily living

Table 2-6 Summary of the main findings of the studies included in the review

2.4.7 Interventions

Two of the five studies investigated punctum plugs for dry eyes (Mansour *et al.*, 2007; Qiu *et al.*, 2013). One study investigated acupuncture for dry eyes (Lin *et al.*, 2015) and another silicon hydrogel contact lenses for dry eyes (Li *et al.*, 2015). One study investigated an intraoral lubricating device for dry mouth (Frost *et al.*, 2006), another investigated acupuncture for dry mouth (List *et al.*, 1998), another investigated laser acupuncture for dry mouth (Cafaro *et al.*, 2015) and the final study investigated psychodynamic group therapy (Poulsen, 1991).

2.4.8 Outcome measures

A wide range of outcomes were assessed and this is reflected in the outcome measures used. Seven studies measured a range of outcomes relating to dryness (List *et al.*, 1998; Frost *et al.*, 2006; Mansour *et al.*, 2007; Qiu *et al.*, 2013; Cafaro *et al.*, 2015; Li *et al.*, 2015; Lin *et al.*, 2015). These included the following clinician reported outcomes of; unstimulated salivary flow over 5 minutes (Cafaro *et al.*, 2015) 10 minutes (List *et al.*, 1998; Frost *et al.*, 2006; Mansour *et al.*, 2007; Qiu *et al.*, 2013) and over 15 minutes (List *et al.*, 1998) and paraffin stimulated salivary flow over 5 minutes (List *et al.*, 1998). Further physician reported oral dryness measures included the use of a 1-13 clinical dryness scale (Frost *et al.*, 2006) and oral bacteriological sample and periodontal measurements (pocket depth, plaque and bleeding) (Frost *et al.*, 2006). Clinician reported assessments of ocular dryness included; tear gland function tests including Schirmer test (Mansour *et al.*, 2007; Qiu *et al.*, 2013; Li *et al.*, 2015; Lin *et al.*, 2015), Rose Bengal test and mucus debris in the cul-de-sac (Mansour *et al.*, 2007) and tear break up time (Qiu *et al.*, 2013; Li *et al.*, 2015; Lin *et al.*, 2015), ocular contrast sensitivity (Qiu *et al.*, 2013), glare disability (Qiu *et al.*, 2013), corneal fluorescein staining (Qiu *et al.*, 2013; Li *et al.*, 2015) and tear meniscus depth, height and area (Lin *et al.*, 2015).

Participant reported outcome measures for dryness included discomfort from mouth dryness, eye dryness and tongue and mouth burning (10 point visual analogue scale (VAS)) (List *et al.*, 1998) and subjective ocular discomfort (Mansour *et al.*, 2007; Li *et al.*, 2015; Lin *et al.*, 2015).

Functional outcomes included a participant reported questionnaire regarding the ability to speak, chew and swallow (Frost *et al.*, 2006), a 10 point VAS on both perceived global reduction in activities of daily living (ADL), ability to chew and swallow (List *et al.*, 1998). Two studies collected data on visual function (Li *et al.*, 2015; Lin *et al.*, 2015) but in both of these studies, these were included as part of a total score of subjective symptoms and the functional data were not reported separately. A further study used a speech test where the phoneme sequence 'PUTTICA' was repeated as many times as possible over a 2-minute period (Frost *et al.*, 2006).

2.4.9 Adverse events

No serious adverse events were reported. One of the studies on punctum plugs reported spontaneous plug extrusion in 28% of the participants (Mansour *et al.*, 2007). One participant withdrew from the silicone hydrogel contact lense group in one study (Li *et al.*, 2015) due to not being able to tolerate the lenses. One study reported a higher rate of drop out in the acupuncture intervention group than the artificial tear group (Lin *et al.*, 2015). This might imply an issue with acceptability in the acupuncture group, however acceptability of this intervention was not formally measured.

2.4.10 Effects of interventions

2.4.10.1 Primary Outcomes: Activities

Oral lubrication devices

Frost et al (Frost *et al.*, 2006) examined speech function but did not present baseline data, therefore it is impossible to ascertain whether the difference observed between the two groups was due to the intervention as there may have been a difference at baseline.

Psychodynamic group therapy

Poulsen (Poulsen, 1991) used the Arthritis Impact Measurement Scale (AIMS) before and after psychodynamic group therapy. The AIMS is a self-reported questionnaire on physical functioning. However the author did not report the actual results, and I am therefore unable to comment on the reliability of their claim of positive effect.

Acupuncture

List et al (1998) asked patients to report the degree in reduction on their speech and chewing on a VAS scale at baseline and after a 10 weeks course of acupuncture. There was no significant difference between the control group and the intervention group at 10 weeks. In addition, participants in the same study were asked to report a global estimate of the reduction in daily activities on a scale of 0 to 10 with '0' meaning 'not at all' and '10' meaning 'extreme'. However, again there were no significant differences between the intervention group and control groups after 10 weeks.

Participation

The study by Poulsen (Poulsen, 1991) was the only one which measured participation as an outcome and found no improvement in participation.

2.4.10.2 Secondary Outcomes: Impairments of body functions and structures

Punctal plugs

Mansour et al (Mansour *et al.*, 2007) asked participants to score eye discomfort on a 1 to 10 scale in both eyes. These measurements were taken at baseline and at follow up, approximately six weeks after a silicone punctum plug was inserted into one of the eyes. However as the scale used was not validated, it was unclear how the scoring was conducted and the sample size was very small (n=13). Furthermore, the authors did not report significant differences between the control eyes and the plugged eyes.

Qui et al (Qiu *et al.*, 2013) conducted a Schirmer I test to determine dryness of the eyes before and after treatment and both groups improved. Although the authors claim the plug group improved significantly more than the artificial tear group, they did not present the analysis that support this claim. Qui et al (Qiu *et al.*, 2013) also examined glare disability and visual acuity (ability to discriminate between two objects). Both the artificial tears and punctal plug groups demonstrated improvement for these two outcomes, but there was no significant difference between the two groups.

Contact lenses

Li et al.'s study (2015) found no differences in visual acuity between participants wearing silicone hydrogel contact lenses and those in the control group using autologous serum at any of the time points during the course of the study.

Li et al.'s (2015) study also reported significant improvement in subjective eye discomfort scores for the group who received the contact lens intervention. These scores were significantly better than the group who receiving autologous serum eye drops at all time scales following the start of treatment, including 6 weeks following the withdrawal of the intervention. There were no significant improvements in tear production following the contact lens intervention. Although tear break up time did

improve following wear of the contact lenses, these improvements were no greater than the improvements seen in the eye drop intervention group. Corneal staining revealed significant reduction in the staining areas at all time points following the introduction of the contact lenses. These improvements were significantly better than improvements measured in the serum eye drops group and were maintained at 6 weeks following the withdrawal of the lens treatment.

Oral lubrication devices

Frost et al (Frost *et al.*, 2006) presented no baseline data, therefore their results were not interpretable.

Psychodynamic Group therapy

Poulsen (Poulsen, 1991) reported improvements in alexithymia scores nine months after taking part in psychodynamic group therapy, despite not measuring the scores at baseline for the intervention group.

Acupuncture

List et al (List *et al.*, 1998) asked participants to evaluate mouth dryness, eye dryness and burning sensation in the mouth on a VAS scale at baseline and after a 10 week course of acupuncture but there were no significant differences between the intervention and control groups.

Lin et al (2015) reported no significant differences in subjective ocular symptoms using a validated measure after a course of acupuncture for dry eyes (the Ocular Surface Disease Index (Schiffman *et al.*, 2000)). This measure included as score for environmental triggers, and these environmental factors were not reported separately. The sample size was very small in this study (n=18) meaning that although the results were non-significant, the study was probably insufficiently powered to detect an effect.

Laser acupuncture

Cafaro *et al.* (2015) reported a significant increase in salivary flow rates following a course of laser acupuncture for dry mouth. They found significant differences in salivary flow rates between the laser acupuncture intervention group and those receiving the placebo immediately following the intervention and at 30, 90 and 180

days following the discontinuation of treatment. However sample size of the study was low (n=26) and the mechanism of action unclear.

2.5 Discussion

Overall, the quality of most of the included studies was poor. There was high risk of bias in most and none had conducted power calculations. Furthermore, the sample sizes used were small, meaning the studies were likely to be underpowered to detect an effect size that is predicted to be modest. The outcome data from studies included within this review could be used to determine power calculations for well-conducted multi-centre randomised controlled trials of the interventions.

The quality of reporting was also poor in many of the studies, including the data presentation, which makes data interpretation difficult. For example no differences between study baseline and endpoint scores were reported in two of the studies (Poulsen, 1991; Frost *et al.*, 2006) and one of these reported improvement in an outcome but presented no supporting data (Poulsen, 1991).

The studies did not conduct the appropriate analysis of change in scores, or the analysis of difference between the two groups. Instead, baseline to study endpoint scores were reported. The exception was Li *et al.* (2015) who did conduct the appropriate analyses.

In terms of individual studies, the studies by Lin *et al.* (2015), Cafaro *et al.* (2015) and Li *et al.* (2015) were of poor quality and were probably under-powered. Although Lin *et al.* (2015) did not find any differences between the groups in response to the acupuncture, this study had such small numbers of participants that the intervention may have effects that were not detected by this study. On the other hand, although Cafaro *et al.* (2015) found that their laser acupuncture group had a positive response to the intervention, the small numbers of participants in their study means it is possible that the result could be due to a type 1 error (in which a positive result is detected by chance). Li *et al.*'s (2015) study did make comparisons between groups, but did not describe their randomisation methods or make it clear whether the person taking the measurements was blinded to the intervention group. Blinding of the assessor is unlikely as those in the contact lens group wore the lenses continually. Therefore, the results of this study were at risk of bias at many levels.

None of the studies measured quality of life, self-efficacy, adverse events or further environmental factors such as carer strain and costs. Furthermore, some of the included studies used outcome measures, which are not standardised or even necessarily appropriate for PSS patients. Recent advances in PSS research have resulted in more relevant outcome measures being developed (Cornec *et al.*, 2015; Rischmueller *et al.*, 2016; Seror *et al.*, 2016), which might be used in future trials of non-pharmacological interventions.

The comparative groups used in each study varied. Some did not use a placebo group at all. Furthermore, since there is not yet a 'standard' non-pharmacological treatment for PSS, (Price, 2016a) a comparison between two or more groups receiving an active treatment does not necessarily tell us anything useful. This is because each intervention might be equally effective.

Overall, my findings were inconclusive. There are suggestions from these studies that punctal plugs are effective for outcomes of lacrimal gland function outcomes. This is in line with a Cochrane review of punctal plugs in dry eyes (Ervin *et al.*, 2010), which was not PSS specific. The oral lubrication devices, psychodynamic therapy and acupuncture did not provide evidence of significant benefit. However, given the poor quality of the data presented and the small sample size, we cannot be certain that these interventions provide no benefit either.

The studies included some measures of glandular function including saliva production and some measures of activities. Of the activity measures, not all related to everyday life. An example is the PUTTICA speech test (Frost *et al.*, 2006), which is a surrogate outcome with an unclear relationship with ease of speech. Furthermore, not all outcome measures were standardised and were not all necessarily appropriate for PSS patients. Only one study looked at any aspects of participation (Poulsen, 1991) and there seems to be a lack of appropriate outcome measures which are relevant to patients in terms of activity and participation. Studies investigating outcomes of body function and structures need to determine the relevance of these outcomes to patients and investigate the impact of such symptoms on participation, the ability to perform daily activities and quality of life.

I discovered no published reports of randomised controlled trials of studies looking at exercise or cognitive behavioural therapy, which have been examined in chronic fatigue syndrome (White *et al.*, 2011). A small study investigating a group aerobic exercise intervention (Nordic walking) (Strombeck *et al.*, 2007) was not included as participants were not randomised and as previously mentioned, it is difficult to determine evidence of efficacy in non-randomised trials (O'Connor *et al.*, 2008).

Through a search of clinical trials databases I was able to determine that there were 3 relevant clinical trials (Table 2-4) which have yet to publish their results. This includes a randomised controlled trial registered in The Netherlands, investigating cognitive-behavioural therapy and exercise training to treat fatigue in patients with Sjögren's and non-Sjögren's sicca syndrome (van Leeuwen, 2012); an exercise intervention registered in Brazil (Miyamoto, 2015) and a study of eyelid debridement in Canada (University of Waterloo, 2014). Further research is recommended into clinically relevant non-pharmacological interventions where there is evidence of efficacy in other conditions with similar symptoms; such as cognitive behavioural therapy and graded exercise therapy for fatigue management in patients with chronic fatigue syndrome.

A Cochrane systematic reviews of punctal plugs for dry eyes concluded that they provided some symptomatic relief in severe dry eyes (Ervin *et al.*, 2010) and it is likely that they would be of benefit in PSS as well as other dry patient groups. Further investigation into any differences between PSS dry eye treatment and standard dry eye treatment is warranted. A further Cochrane review concluded that there was low quality evidence that acupuncture was no better than placebo for dry mouth symptoms in mixed patient groups and there was insufficient evidence to support the use of electro stimulation for oral dryness (Furness *et al.*, 2013). Further studies for these interventions are also therefore warranted.

None of the studies measured quality of life, self-efficacy, adverse events or further environmental factors such as carer strain and costs. Furthermore, some of the outcome measures used outcome measures which had not been standardised or shown to be appropriate for PSS patients.

2.6 Conclusions

Overall, I identified no current evidence to support any non-pharmacological interventions to improve PSS. The area of research needs good quality, appropriately powered RCTs that are reported according to CONSORT guidelines (Schulz *et al.*, 2010). Outcomes should be sensitive to changes that are important and relevant to patients including functional and participatory outcomes.

Interventions are required to support patients with this disease to be able to participate more fully in daily life by being able to undertake valued life activities and taking on roles of their choosing. With no known evidence based interventions to support patients in this regard, the development of such interventions is a priority.

2.7 Summary

I conducted this systematic review to determine whether there are any non-pharmacological interventions which are likely to improve participatory and functional outcomes for PSS patients. The results of this review were inconclusive as there was not enough evidence to either support or refute non-pharmacological interventions.

Prior to designing any further interventions to improve function and participation for PSS patients, it is essential to determine what prevents people with the disease from doing valued life activities which they need or want to do. In the next chapter I conduct a study where barriers to activity and participation are identified by stakeholders with the lived experience of PSS (patients and family members) and clinicians who treat PSS patients.

Chapter 3. A group concept mapping study identifying barriers to participation and performing daily activities

The previous chapter demonstrated that there was little evidence for non-pharmacological interventions and studies included within the systematic review gave little attention to functional or participatory outcomes. Interventions should target barriers identified by people with an understanding of the disease, either objectively or through their lived experience. Of the identified barriers or intervention targets, the ones perceived to be of most importance by stakeholders provide an ideal starting point. This chapter reports the methods and results of a group concept mapping study, where stakeholders with a lived experience of PSS and stakeholders who treat PSS patients in clinical settings were asked to identify important barriers to participation and performing daily activities for people with PSS.

3.1 Aim and objectives

The aim of this study was to determine important key factors or barriers affecting participation and ability to perform daily activities for people with PSS and to identify factors perceived to be feasible to change.

The objectives were achieved through the collection of data from different stakeholder groups: Patients with PSS, adult household members (AHMs) (i.e. adults who live with a person with PSS) and health care professionals (HCPs) who see patients with PSS in their clinical settings. The objectives were as follows:

- i. Identify barriers to participation and being able to perform daily activities for people with PSS by completing a brainstorming exercise with stakeholders
- ii. Structure the generated ideas into clusters or themes through a sorting exercise
- iii. Identify the most important themes and promoters through a rating exercise and to identify which areas participants perceive to be feasible intervention targets
- iv. Compare similarities and differences in priorities between different stakeholder groups

3.2 Methodology

3.2.1 Justification of chosen methodology

I chose group concept mapping (GCM) methodology, to achieve the aims and objectives of this study. GCM was developed by Trochim (Trochim, 1989) and is a mixed-methods participatory approach which uses a combination of group processes (brainstorming, sorting, rating and interpretation) and a sequence of multivariate statistical analysis (multidimensional scaling and hierarchical cluster analysis) that result in visual representations of all stakeholders opinions in the form of concept maps, pattern matches and go-zones. Priority values are added by participants to qualitative statements gathered during the brainstorming phase and these can be interpreted in pattern matches and go-zones and used in planning or evaluation studies (Kane and Trochim, 2007).

An advantage of GCM over some other methods is that it is an equitable process, giving an equal voice to all stakeholder groups and does not direct participants to form a consensus. Qualitative interviews and focus groups with stakeholders were considered as alternative approaches. These methods can be used to collect detailed description about a topic and can give very useful insights (Weiner *et al.*, 2011). Unique ideas which have been identified during interviews or focus groups can be grouped using thematic analysis (Braun and Clarke, 2014). However, thematic analysis has limitations, as it is subjective; it is conducted by a small number of researchers and can be subject to bias. Furthermore results from qualitative methods are not easily quantifiable (Anderson, 2010). These drawbacks mean that it would be very difficult to quantifiably prioritise promoters and compare priorities between stakeholder groups using purely qualitative methods.

Surveys are a tool which can be used by participants to rank predetermined ideas, e.g. with a Likert scale (Likert, 1932). When using this approach, it is important to ensure that all concepts are captured within the survey to prevent missing any important ideas (Burns *et al.*, 2008). Open-ended survey responses provide an alternative way to collect new ideas, at low cost and from large numbers of participants. This type of survey also offers greater anonymity than other qualitative approaches and may elicit more honest approaches (Erickson and Kaplan, 2000). However, participants who have completed the survey do not usually contribute to the thematic analysis in this method and the qualitative analysis is again, subject to increased bias.

Delphi methods offer an alternative solution, as the results are quantifiable. However the methods were developed with the purpose of producing consensus of opinion between experts (Dalkey and Helmer, 1963). Delphi methods cannot therefore be used to identify similarities and differences in opinion between different stakeholder groups.

GCM draws on the advantages of both qualitative and quantitative approaches. It allows participants to contribute their ideas until data saturation is achieved. Multi-dimensional scaling (MDS) and hierarchical cluster analysis reduce risk of bias as every participant who completes the sorting exercise takes part in the thematic analysis and their opinion counts. The resulting concept maps are therefore co-authored by all participants. Key priorities can be identified through the analysis of participants' rating data and comparisons can be made between stakeholder groups. Furthermore, comparisons within stakeholder groups can be made, for example between patients, between younger and older patients or between doctors and therapists.

In the rheumatology field, GCM has been used to design and develop interventions such as an online arthritis pain management programme (Trudeau *et al.*, 2010), to prevent work disability in rheumatoid arthritis patients (Varekamp *et al.*, 2005) and to understand their work requirements (Detaile *et al.*, 2003). It has also been used to support the development of interventions in areas such as HIV/AIDS (Abdul-Quader and Collins, 2011) and public health, including health interventions for immigrants (Vaughn *et al.*, 2016) and community relevant physical activity interventions (Kelly *et al.*, 2007).

3.2.2 Description of concept maps

Concept maps consist of point maps, cluster maps and cluster rating maps. Pattern matches and go-zones can also be generated from the software. A brief explanation for each term follows and a more detailed explanation provided in the results section in this chapter (Section 3.4).

A **point map** is a visual representation of how all stakeholders have sorted their statements and is determined by the multidimensional scaling analysis. Each statement is represented by a point on the map.

A **cluster map** shows the groups of statements as themed clusters and is generated following hierarchical cluster analysis.

A **cluster rating map** demonstrates how a group of participants prioritise each cluster. Higher priority clusters have more layers (up to five) and clusters which are given lower ratings contain as few as one layer.

A **pattern match** is a visual result demonstrating how different stakeholder groups' opinions agree or differ about groups of ideas or clusters of statements.

A **go zone** is a bivariate scatterplot, demonstrating how two different groups of stakeholders have rated the statements in a concept map, either at a cluster level or for all the statements within the concept map. Statements falling within the top right quadrant of the go zone have been given above average priority ratings by both groups. The quadrants are determined by the mean ratings for each of the comparative groups. These go zone statements are instructive for action planning.

3.2.3 The concept mapping process

GCM follows a distinct five-stage process:

1. Preparation for concept mapping: The key issue is identified, then a 'focus prompt' is developed and participants are identified.
2. Idea generation: A brainstorming exercise takes place with stakeholders who have an interest and expertise in the area. Participants are each asked to provide their individual ideas in response to the focus prompt.
3. Structuring the ideas: A refined list of statements from the brainstorming exercise is presented back to participants who are asked to rate each statement and to sort all of the statements into groups of ideas which they perceive to be similar in meaning.
4. Representation: The collected data are analysed using a specialist software. Concept maps, 'pattern matches' and 'go-zones' are produced.
5. Interpretation of the maps.

The protocol for the study was published a-priori (Hackett *et al.*, 2014).

3.3 Method

3.3.1 Stage 1: Preparation for concept mapping

3.3.1.1 Study advisory group

My study advisory group included my supervisory team and two people with PSS who serve on the committee of the local patient North East Sjögren's Syndrome Association (NESSA). Further advice was sought from relatives and friends of patient members of the advisory group when deciding on a final list of ideas following the ideas generation stage. The advisory team contributed at the protocol development stage, during the delivery of the study and during the interpretation stage.

3.3.1.2 Development of the focus prompt

In order to ensure the aim of the study was achieved, an appropriate focus prompt was required. The focus prompt was going to be used in the brainstorming to generate the ideas/statements. It is therefore essential that this prompt was understandable. Many concept mapping studies use an incomplete sentence as a prompt to elicit statement responses from participants (e.g. (McLinden, 2013; Stoyanov *et al.*, 2014; Hackett *et al.*, 2016b). The focus prompt emerged from discussions with members of the study advisory team and with experts in concept mapping during a five-day

concept mapping training course (Concept Mapping Incorporated, Ithaca, New York).
The focus prompt I used in this study was:

***People with Sjögren's could do more of the things they want to do or
have to do if.....***

3.3.1.3 Ethical approval

An ethical application was drawn up and included a study protocol, participant information sheets and participant documents (See Appendices (Section A.1)). The application was submitted for proportionate review and was granted by the Office for Research Ethics Committees Northern Ireland (13/NI/0190, IRAS Ref: 125562). Furthermore the study was accepted onto the National Institute of Health Research Comprehensive Clinical Research Network's (CCRN) Portfolio of non-commercial clinical research studies (Study ID: 15939). Principle Investigators (PIs) from each of the Patient Identification Centres (PIC sites) in England for the UKPSSR (Ng *et al.*, 2011) were contacted by the CCRN to see if they would be interested in supporting the study. 12 PIs agreed and NHS Trust R&D approvals were sought and granted from each of these sites with support from the CCRN.

3.3.1.4 Confidentiality

To maintain confidentiality, each participant was assigned a unique code. Reply slips and consent forms were stored securely in a locked office at the Freeman Hospital, Newcastle upon Tyne NHS Foundation Trust. Electronic records were password protected and stored on an NHS computer. Participants opting to use the online system to complete the concept mapping exercises were allocated a unique username and password to ensure they were not identifiable on the web-based system.

3.3.1.5 Sample size

The recommended minimum number of participants for a GCM exercise is 40 (Rosas and Kane, 2012). In order to enable sub-group analyses and to allow for modest attrition rates (20%) at each step of the GCM exercise, I aimed to recruit approximately n=280 participants. I aimed to recruit 180 patients with PSS, 50 AHMs and 50 HCPs. This would allow me to detect a difference of the same order of magnitude as the background variability with 80% power. Subgroups within the patient group would

allow me to compare opinions of PSS patients with varying levels of fatigue, quality of life (QOL), perceived dryness, pain, cognitive symptoms, and mood disturbances.

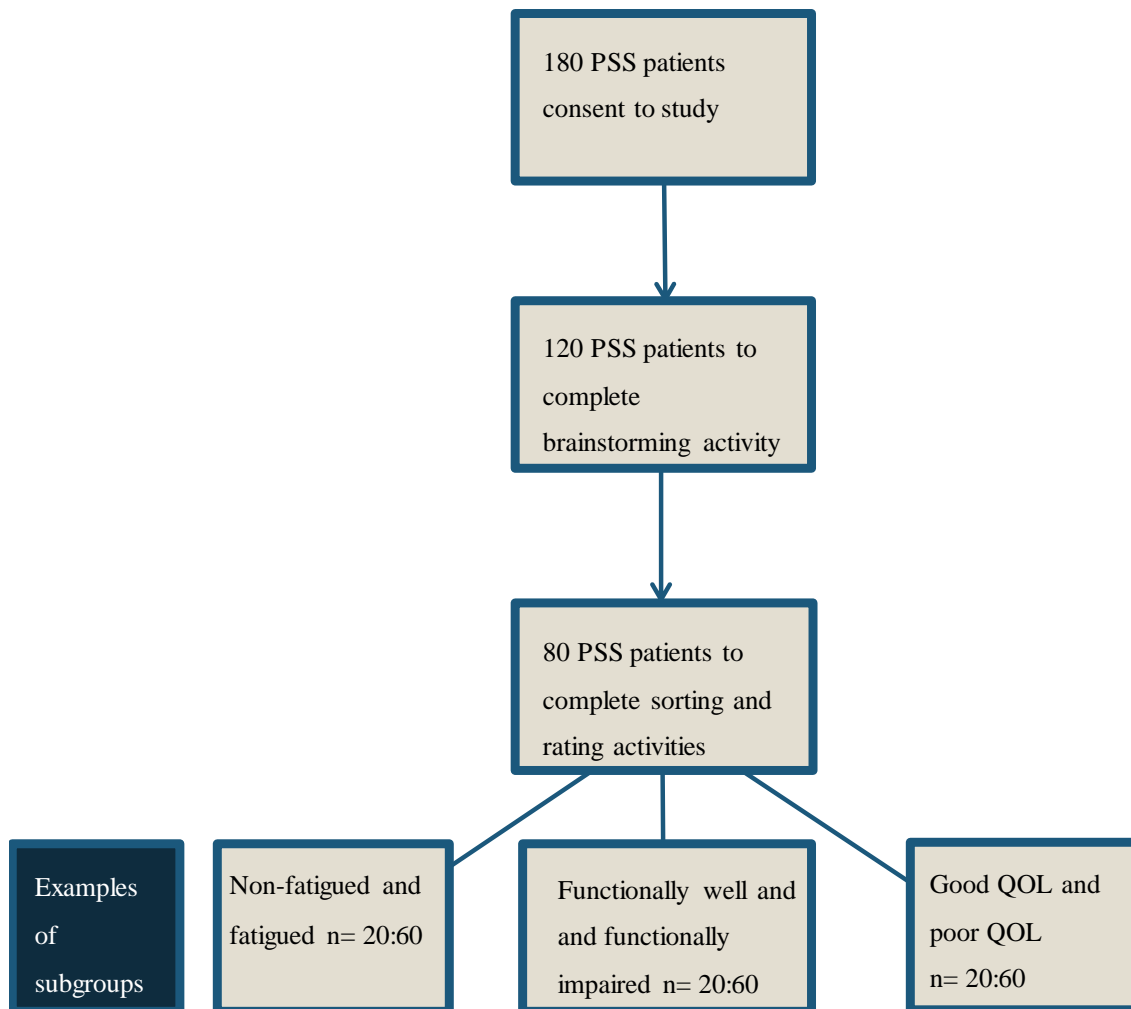


Figure 3:1 The a-priori flowchart of participants to be recruited to the GCM study, including estimated attrition rates at each step of the GCM process

3.3.1.6 Recruitment

The UKPSSR is a large database of patients recruited from different parts of the UK. All participants of the UKPSSR have provided their consent to be contacted for further research.

Patients from the UKPSSR were invited to take part in this study as all participants of the UKPSSR are over 18 and diagnosed with PSS with the American European Consensus Criteria (Vitali *et al.*, 2002). The Patient and Adult Household Member (AHM) recruitment took place from 12 sites across England from February to August 2014 via postal invitation. The location of the sites is shown in

Figure 3:2. Within each invitation pack posted out to the potential participants was an envelope containing an invitation pack labelled 'for the attention of an adult household member'. Health Care Professionals (HCPs) were invited to participate at professional meetings including a rheumatology staff meeting at the Freeman Hospital, Newcastle upon Tyne and a regional Primary Care Research Meeting in Gateshead. Health care professionals were contacted via email distribution lists, including a list of UKPSSR collaborators, a regional rheumatology email distribution list and the College of Occupational Therapists Specialist Subsection – Rheumatology email list. Informed consent was obtained from all participants according to the principles of the Helsinki Declaration.



Figure 3:2 Participant identification centre sites from where PSS and AHM participants were recruited

3.3.1.7 Completion of the concept mapping study

Participants were given the option of completing all stages of the concept mapping study on paper via the post, in prepaid envelopes or online after logging onto a web-page using a unique username and password.

3.3.1.8 Data collection

Baseline demographics were collected from all participants. PSS patients and AHMs were asked to provide the following demographic information; age in years, gender, employment status, how long in years they have had a diagnosis of PSS or how many years had the person they live with has had a diagnosis of PSS. In addition PSS patients were asked to indicate if there were any further adults in the household, if they had any dependents, if they had paid for private therapy or complementary therapies in the past 6 months, level of education, household income, and whether they were in receipt of benefits. The PSS group also completed visual analogue scales for pain and fatigue and the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1986), the Cognitive Failures Questionnaire (Cogfail) (Broadbent *et al.*, 1982) and a measure of

functional ability - the Improved Health Assessment Questionnaire (Improved HAQ) (Fries *et al.*, 2009). The Improved HAQ consists of 20 questions which ask respondents to rate their ability to perform daily activities on a 5-point scale, where 0 = without any difficulty and 4 = unable to do. These questions are divided into 8 domains of physical function: dressing, arising, eating, walking, hygiene, reach, grip, and activity. The highest scoring question in each domain is used as the domain score. The total Improved HAQ score = ([mean domain score] × 25). Higher scores indicate greater functional impairment.

Finally, PSS participants also completed the quality of life measure SF-36 version 2 (Ware, 2000; Ware *et al.*, 2000). SF-36 norm-based scores were calculated using United States (US) normative data as the Quality Metric Health Outcomes™ Scoring Software provided with the SF-36 licence uses the US normative scores to create these scores. It was a pragmatic decision to calculate normative scores rather than the actual scores as it is then possible to make comparisons between the results for each domain, between groups and with other population groups. The drawback is that there may be slight variations between the US and United Kingdom normative scores. However, a previous study on the original SF-36 demonstrated that there is little difference between the UK and US norms (Jenkinson, 1999). Furthermore, the Quality Metric Software works out a norm-based score for participants individually, based on their age and gender. I could have also compared the actual SF-36 scores with UK population norms, but a direct comparison would have been made at a group level, rather than making paired comparisons, and the participant scores would not have been made in direct comparison with norms of the same age and gender. The purpose of collecting both the demographic and symptom data was to provide an in depth description of the population.

Family members were asked to complete short validated questionnaires to measure the impact of their spouse/relative's disease on them. These measures included the Caregiver Strain Index (CSI) (Robinson, 1983) and the SF-36 version 2. The CSI is a thirteen item scale and respondents are asked to respond with a 'yes' or 'no' to each item. A score ≥7 out of 13 indicates high carer strain. Again, the purpose of collecting this information in addition to the demographic data, was to provide an in-depth description of the AHM population.

HCPs were asked to indicate which professional group they belong to so comparisons could be made between different health care professional groups. These data therefore allowed additional subgroup analyses within the family and provider groups.

PSS patient participants (n=122) were identified from 12 NHS sites in England. They were all participants in the United Kingdom Primary Sjögren's Syndrome Registry (Ng 2011) and as such fulfilled the American European Consensus Group (AECG) diagnosis criteria. Inside their postal invitation was an invitation to an adult household member (AHM). 43 AHMs took part in this group concept mapping study. In addition health care professionals (HCPs) who see PSS patients were invited to participate via email distribution lists and at professional meetings and 67 took part. The concept mapping study consists of three distinct stages. Not all participants undertook every stage. PSS patient and AHM participants were given the option of attending a face-to-face brainstorming meeting if they lived close-by to the meeting venue. All participants were given the option of completing the GCM exercises online via a web-based interface (Concept Systems Global MAX™) or on paper via the post.

3.3.2 Idea generation

3.3.2.1 Brainstorming

In the first stage of the study participants were asked to complete the following sentence as many times as they could:

"People with Sjogren's could do more of the things they want to do and have to do if....."

Participants completing this exercise online or in a face-to-face meeting could see statements written by other participants meaning that duplication might be less than when completed in on paper, with no access to other participants' responses.

Brainstorming continued until data saturation was achieved (Trochim, 1989; Kane and Trochim, 2007). This was the point where no further unique ideas were being generated through the brainstormed responses (de Kok *et al.*, 2007). The resulting statement set was reduced to a shorter list of unique ideas using a process described by Kane and Trochim (2007):

In the statement reduction process each statement was first given a key word. If more than one idea was contained within a statement, the statement was split. For example the statement *“there was a structured support network from other patients and health care professionals which could be accessed when specific needs arose”* was divided into two statements: *“There was a structured support network from other patients”* and *“health care professionals could be accessed when specific needs arose”*. These were then coded separately using an excel spreadsheet. I met with two members of my supervisory team (TR and VD) and the codes were verified. An example of a key word with statements which are very similar in meaning is:

Key word: *Active*

Statements: *i) They keep their body active ii) They keep as active as possible*

At this stage duplicate statements were removed and I checked the statements for syntax and grammar. The wording was changed minimally for some of the statements to ensure they made sense and the grammar and syntax corrected when necessary. However care was taken to ensure that the meaning of the original statement was not lost. For example, the statement *“Healthcare professionals knew about Sjogren’s”* was changed to *“There was education on Sjogren’s for healthcare professionals”*. Any changes to the wording were checked with two supervisors (TR and VD) prior to the study advisory group meeting.

Next, I grouped all remaining statements with the same key word together and listed the key words in alphabetical order in a Word document. The study advisory group met to decide which statements should be included in the final statement set and to discuss the wording of the statements. One patient study advisory group member was present at this meeting and four members of my supervisory team. Another patient, two AHMs and the remaining member of my supervisory team received the list separately and provided feedback via email. Groups of statements which had the same keyword were considered in turn. This process resulted in a synthesised statement list of 94 unique ideas which were reviewed independently by a small group of PSS and AHM representatives.

The set of 94 refined statements were printed individually onto cards and packs of the cards were made up containing one of each statement.

3.3.3 Structuring the ideas

3.3.3.1 Sorting the ideas

Participants were instructed to sort the statements into themes in a card sorting activity. Each statement from the refined list was given a number and printed on a separate card. Participants were asked to sort the cards into groups or piles that were similar in meaning in a way that made sense to them. A sort recording sheet was provided and participants were instructed to give each pile a name and to record the statement numbers in each pile. The online option entailed a similar process with a drag and drop facility within the software.

3.3.3.2 Prioritising the ideas

Participants were asked to rate each statement for importance on a Likert 1-5 scale. The instructions were “rate each statement below on how IMPORTANT you think it is by putting a circle around a number”. 1 on the rating scale represented “relatively unimportant” and 5 “extremely important”.

3.3.4 Representing the ideas

3.3.4.1 Analysing the data

Demographic, clinical and social scores were analysed in Minitab 17 and Graphpad Prism 6. Data distribution was classified as normal or non-parametric by plotting and interpreting histograms alongside the Anderson Darling normality test. Where data were considered as being normally distributed, they are summarized with mean and standard deviation (SD). Non-parametric data are described with a median and interquartile range (IQR). To determine whether SF-36 scores were comparable with the 1998 United States (US) published norms, the norm-based scores were calculated in Quality Metric software and one sample t-tests were then calculated in Minitab 17 with the hypothesized mean of 50 and a confidence level of 95%. Parametric tests were applied to the SF-36 data irrespective of the data distributions as a large population study has demonstrated that the choice of statistical approach has no influence on results for these scores (Torrance *et al.*, 2009).

The GCM analyses were performed using Concept Systems Global Max™ software, specifically designed for GCM projects. Multidimensional scaling techniques were

performed on the card sorting data, which had been arranged into a similarity matrix to position each statement in relation to each other as a point on an x-y axis. This generated a point map with each point representing a statement. Points near to each other on the map will have been sorted together more frequently by participants in the sorting activity in comparison to statements which are further apart. The stress value, a statistic which reflects stability within the overall map was generated. Ideal stress values for concept mapping analyses are below 0.36 (Trochim, 1989).

Secondly, hierarchical cluster analysis was performed using Ward's algorithm created clusters of statements using the multidimensional scaling coordinates (Rosas, 2017; Rosas and Ridings, 2017). In Ward's method, each statement is initially regarded as a cluster. These agglomerate together in such a way as to minimize the variability within a cluster. The software keeps combining clusters by choosing the two clusters which have the shortest distance between their central points until there is only one cluster left. Using a process described by Kane and Trochim (2007), I initially examined the content of 16 clusters and kept combining clusters and their content until there were as few as 4. In this process, the software was used to combine clusters one at a time. The statements within each were examined and interpreted to ensure the statements within conveyed an overall theme for the cluster. This is a qualitative decision and at the point where it no longer made sense to proceed to the next iteration as the contents of the cluster would be too conceptually broad is where the final cluster solution is agreed upon. Using this approach, a final cluster solution was agreed between me and my supervisory team. The software suggests names for the clusters based on the names participants gave to their piles in the sorting exercise and the cluster labels were chosen from these suggestions.

Next, the rating data of the participants were considered. Importance ratings were compared for all participants in a cluster rating map. Next, comparisons in rating data were made between each stakeholder group at cluster level in "pattern matches". The cluster rating map and pattern matches identified the most important clusters from the perspectives of each stakeholder group.

The rating data were next compared in the "go-zones" for each cluster. Go-zones enable examination of rating values for specific statements between two stakeholder groups. There was a high degree of correlation between the rating scores for the PSS

and AHM groups and their data were combined to allow comparisons with the HCP rating scores on the bivariate plot. The mean rating values are used as a cut-off on the go-zones and statements falling within the top right quadrant were considered as being of high importance by both the combined PSS and AHM group and the HCP group. As such, these statements were considered targets for planning future interventions.

3.4 Results

231 participants took part in the study including 121 PSS patients and 43 AHM from 12 sites across England and 67 HCP from across the UK.

From the 371 patients invited to participate in the study 49% replied indicating they would like to take part and overall 33% of patients invited to take part completed one or more stages of the GCM exercise. A flow diagram of PSS patient participants is shown in Figure 3:3.

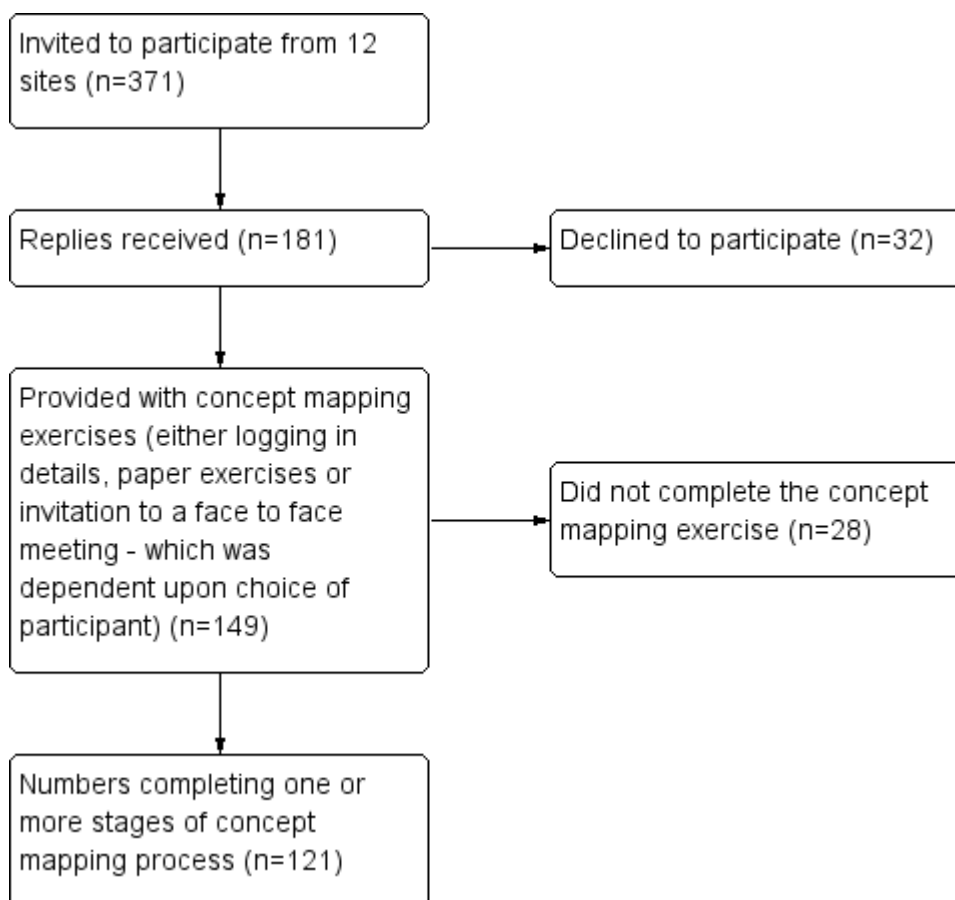


Figure 3:3 Flow diagram of PSS patient participants in the concept mapping exercise

Of the 60 AHMs who consented to take part, 43 went on to complete one or more stages of the GCM exercise (72%). A flow diagram of AHM respondents can be seen in Figure 3:4.

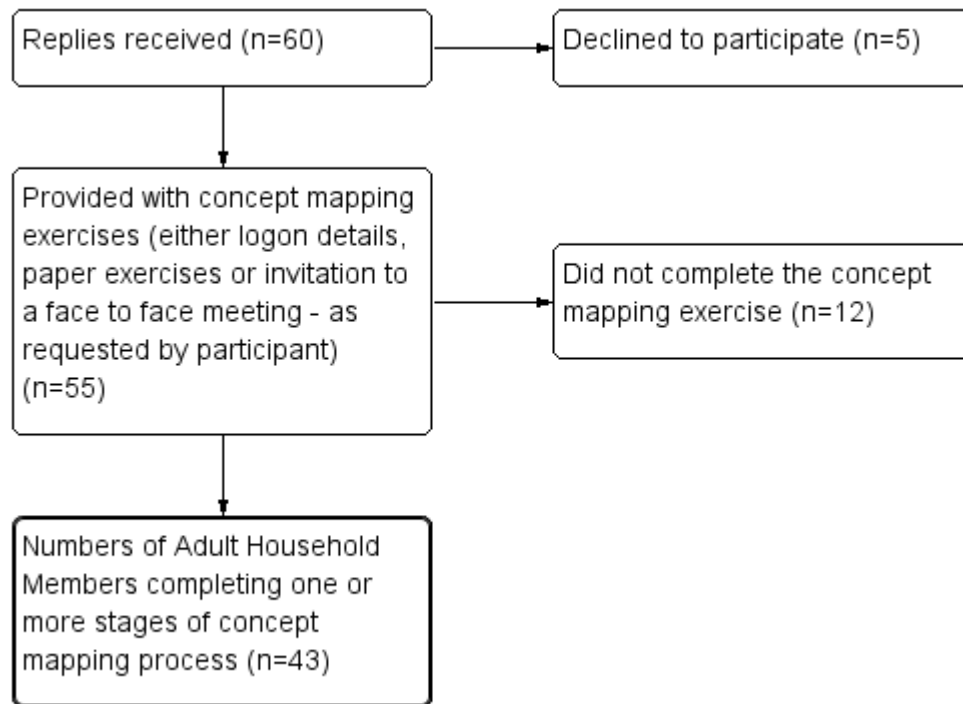


Figure 3:4 Flow diagram of AHM participants in the concept mapping exercise

Of the 70 HCPs who replied to the invitation about taking part in the GCM study, 96% completed one or more stages of the process, meaning 67 HCPs took part in the concept mapping exercise. A flow diagram of the HCP participants is shown in Figure 3:5.

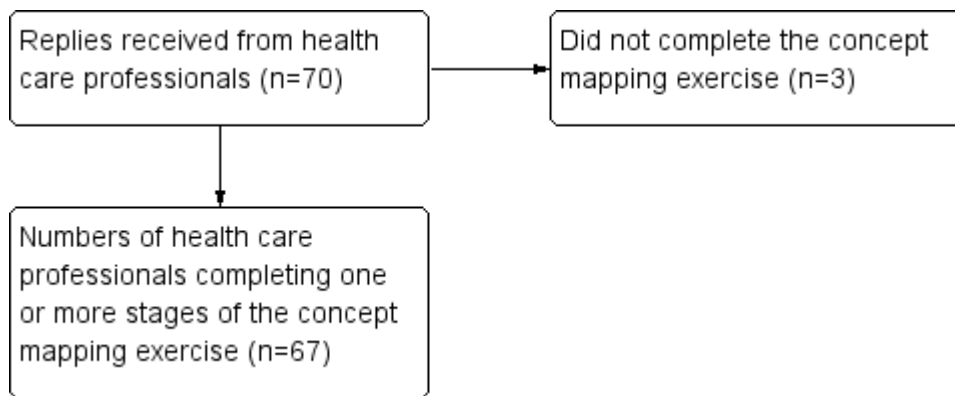


Figure 3:5 Flow diagram of Health Care Professional participants in the concept mapping exercise

The count of PSS and AHM participants who participated in the GCM study at each site is shown in Figure 3:6.

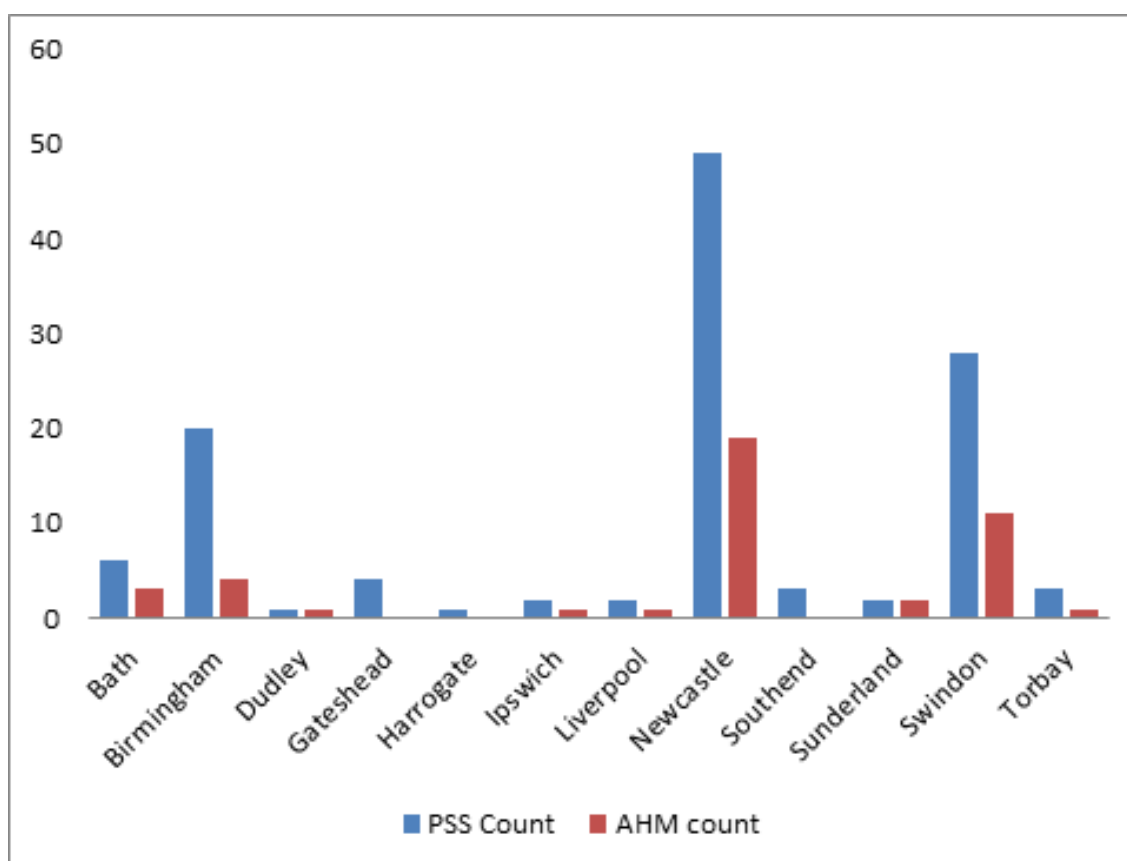


Figure 3:6 Bar chart showing numbers of PSS and AHM who took part in the GCM study from each recruitment site

Newcastle followed by Swindon and Birmingham have the largest numbers of patients recruited to the UKPSSR, which explains why recruitment was highest at these sites. Other sites have fewer registry participants, for example Harrogate had only three UKPSSR participants during recruitment for this study, one of whom opted to take part in the concept mapping study.

A breakdown of the methods participants chose to complete the GCM study are shown in Figure 3:7.

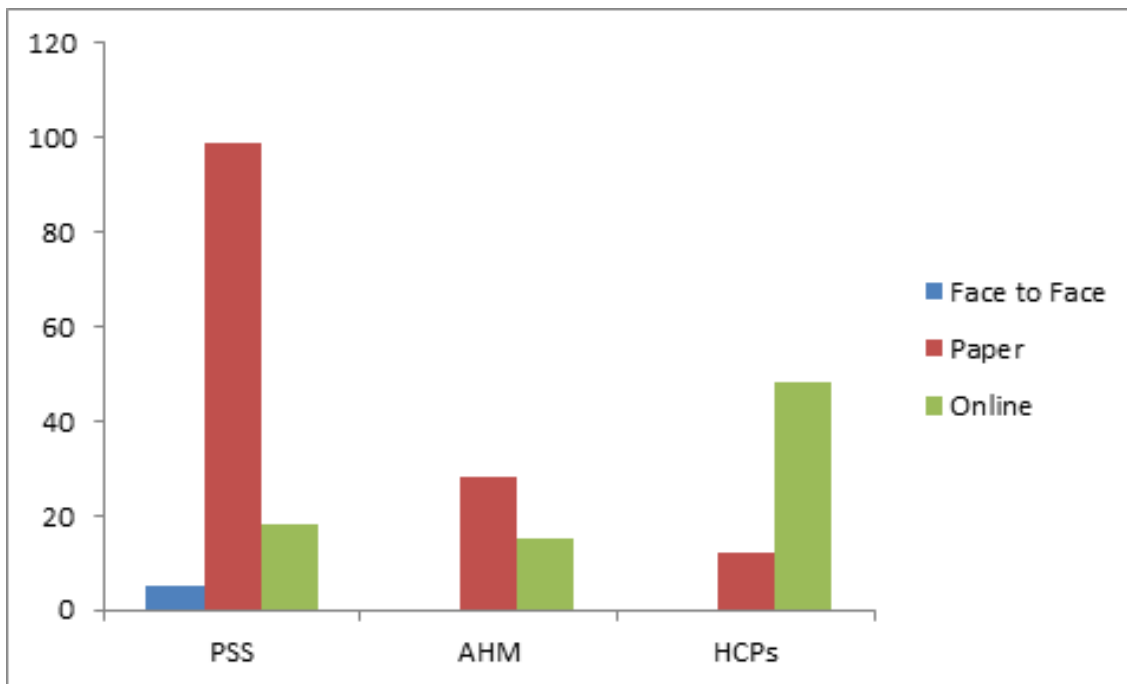


Figure 3:7 Participants who completed the GCM: Method of completion

The majority of PSS patient and the AHM participants opted to take part using the paper method of completion and a small proportion of local PSS patients opted to take part in a face-to-face brainstorming session. The majority of HCPs opted to take part online.

3.4.1 Demographics of PSS participants

A summary of the PSS patient participant characteristics can be viewed in Table 3-1.

The mean age of the AHM participants (n=43) was very similar to the PSS participants at 63.81 (S.D. 9.49). The mean number of years since diagnosis of the people who they lived with who had PSS was also similar to the number of years since diagnosis for the PSS group at 10.41 (S.D. 7.39). 63% of the AHM group participants were male and 37% were female.

		Possible score range	Mean (SD)	Median (IQR)	%
Age			63.01 (9.96)		
Years since diagnosis			10.15 (7.21)		
Gender	Female				86.8
	Male				13.2
Live with another adult	Unknown				0.8
	No				25.6
	Yes				73.6
Dependents at home	Unknown				3.3
	No				81.8
	Yes				14.9
Receiving disability benefits*	Unknown				0.8
	No				77.7
	Yes				21.5
HADs Anxiety		0-21		7 (6)	
HADs Depression		0-21		6 (5.7)	
Pain VAS		0-100	37.3 (27.4)		
Fatigue VAS		0-100	54.6 (29.2)		
Mental Fatigue VAS		0-100	38.1 (28.7)		
Dryness VAS		0-100	56.7 (30)		
Cogfail		0-100	43.2 (18)		
Improved HAQ		0-100		17.2 (36.7)	

*Personal Independence Payment/Disability Living Allowance/Attendance Allowance/Independent Living Fund

Table 3-1 Summary characteristics of the PSS patient participants (n=121)

A breakdown of the employment status of the PSS group data can be viewed in Figure 3:8 below. The proportion of retired participants was similar in both the AHM and PSS participant groups. A larger proportion of the AHM group were in full-time employment compared with the PSS group and a smaller proportion of AHM participants were in part-time work compared with PSS participants.

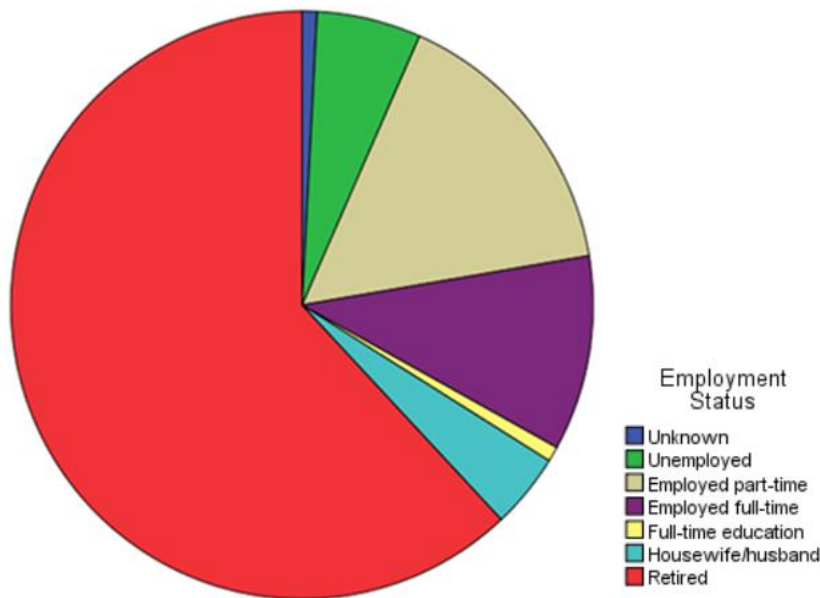


Figure 3:8 Pie chart demonstrating employment status for PSS patient participants (n=121)

The PSS participants had lower quality of life as measured on the SF-36v2 compared with the US norms mean. The PSS SF-36 scores for the PSS participants in comparison to the mean US population norms can be viewed in Figure 3:9.

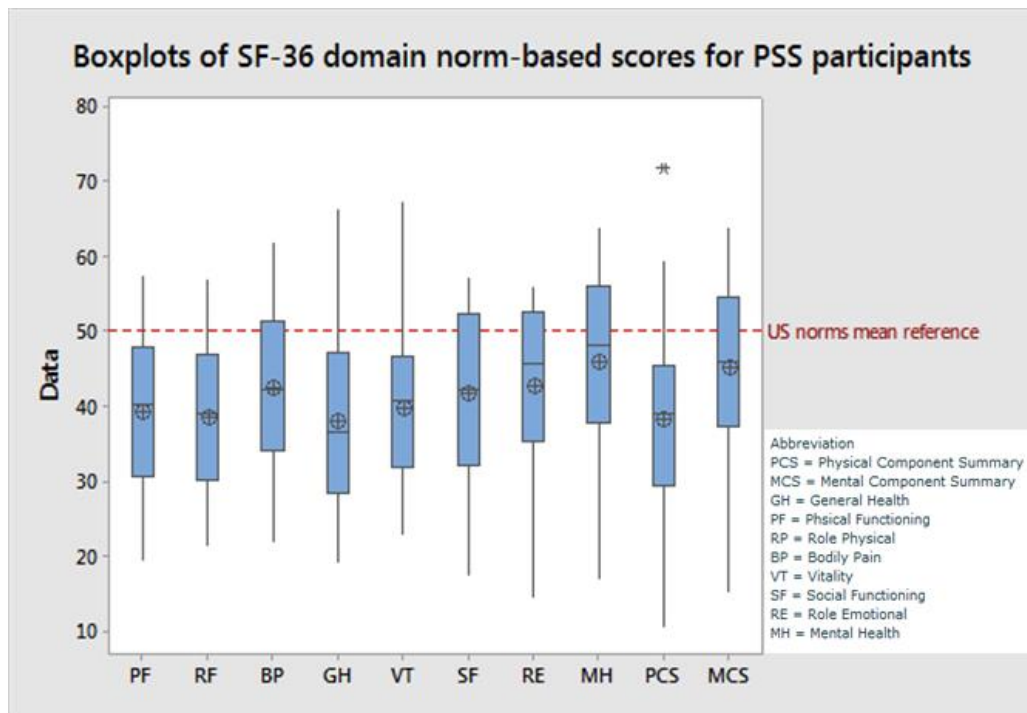


Figure 3:9 SF-36 norm-based scores for PSS patients (n=121)

The PSS patients scored lower than the norm-based scores for all domains of the SF-36. This was calculated as being significant for all individual domains and for the Mental and Physical Component Summary scores (see Table 3-2).

SF-36 domain	PSS Norm-based scores*†	t-value	p-value
Physical Functioning	39.18 (10.88)	-10.94	<0.001
Role Physical	38.36 (10.90)	-11.75	<0.001
Bodily Pain	42.37 (9.93)	-8.46	<0.001
General Health	38.09 (11.94)	-10.97	<0.001
Vitality	39.70 (10.75)	-10.50	<0.001
Social Functioning	41.68 (11.31)	-8.09	<0.001
Role Emotional	42.65 (11.29)	-7.14	<0.001
Mental Health	46.01 (10.71)	-4.08	<0.001
Physical Component Summary	38.15 (11.03)	-11.77	<0.001
Mental Component Summary	45.04 (10.70)	-5.08	<0.001

*Mean (SD) †USA norms mean (SD) = 50 (10) for all domains

Table 3-2 Differences between PSS patient SF-36v2 scores and norm-based scores

3.4.2 Demographics of AHM participants

The proportion of retired participants was similar in both the AHM and PSS participant groups. A larger proportion of the AHM group were in full-time employment compared with the PSS group and a smaller proportion of AHM participants were in part-time work compared with PSS participants. The breakdown of employment status for this group can be seen in Figure 3:10.

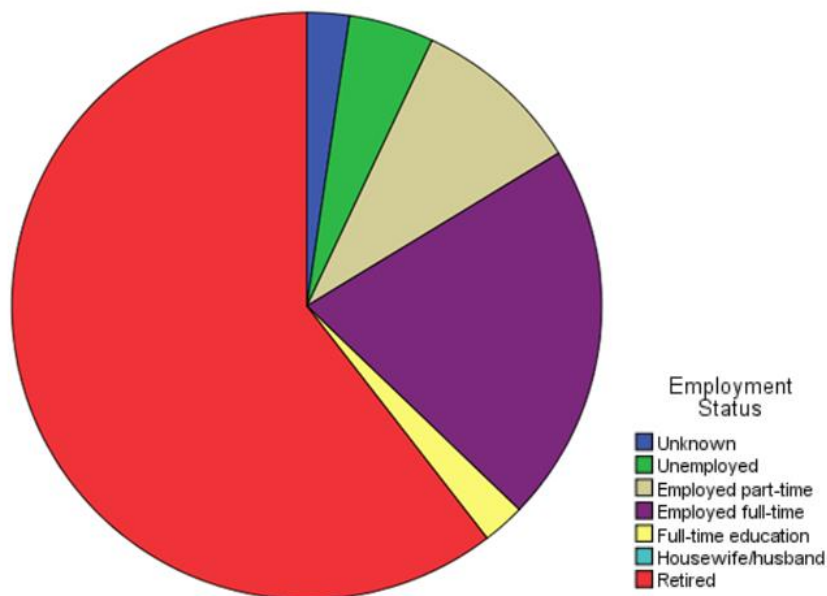


Figure 3:10 Pie chart demonstrating employment status for AHM participants (n=43)

The proportion of retired participants was similar in both the AHM and PSS participant groups. A larger proportion of the AHM group were in full-time employment compared with the PSS group and a smaller proportion of AHM participants were in part-time work compared with PSS participants.

The AHM norm-based SF-36 scores were compared with the US normative data and these can be visualised in Figure 3:11.

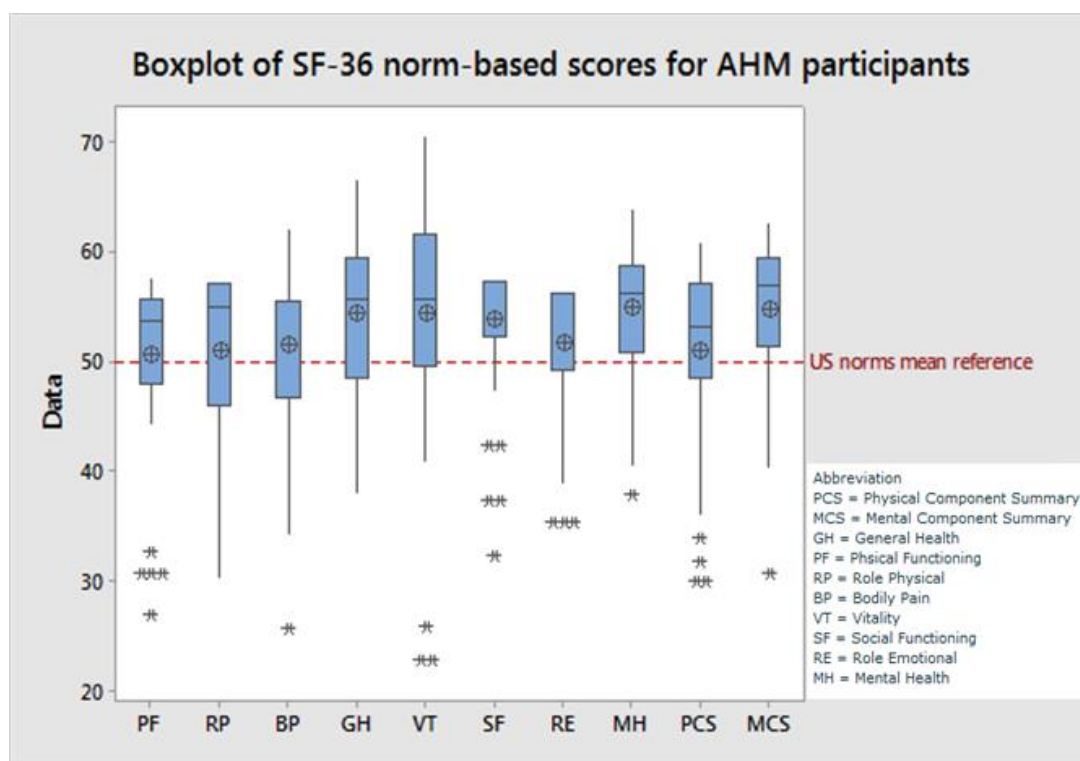


Figure 3:11 SF-36 norm-based scores for AHM participants (n=43)

The comparisons with the normative data mean, using a one sample t-test can be viewed in Table 3-3.

SF-36 domain	AHM Norm-based scores*†	t-value	p-value
Physical Functioning	50.60 (8.28)	0.47	0.639
Role Physical	50.94 (8.23)	0.75	0.456
Bodily Pain	51.41 (9.43)	0.98	0.331
General Health	54.37 (8.15)	3.51	0.001
Vitality	54.33 (10.97)	2.59	0.013
Social Functioning	53.84 (6.61)	3.81	<0.001
Role Emotional	51.63 (6.90)	1.55	0.128
Mental Health	54.88 (6.00)	5.34	<0.001
Physical Component Summary	50.83 (8.75)	0.62	0.539
Mental Component Summary	54.65 (6.95)	4.41	<0.001

*Mean (SD) †USA norms mean (SD) = 50 (10) for all domains

Table 3-3 Comparisons of AHM norm-based scores with US norms

The AHMs had SF-36 scores which were comparable with the US normative data for the Physical Functioning, Role Physical, Bodily Pain and Role Emotional domains as well as the Physical Component Summary. The AHMs scored significantly better than the US norms for the General Health, Vitality, Social Functioning, Mental Health domains and the Mental Component Score.

The caregiver strain scores are shown in Figure 3:12. Although the median CSI score of 1 demonstrates that most AHM participants experienced very little caregiver strain, 14% of AHM participants did experience high levels (indicated with a CSI score ≥ 7).

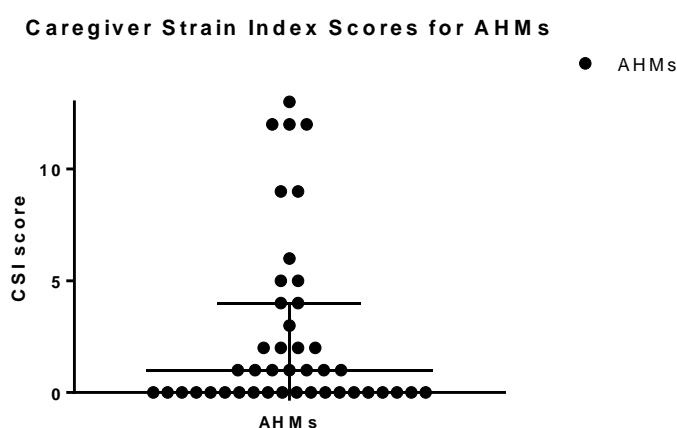


Figure 3:12 Dot plot of Caregiver Strain Index scores for AHM participants (n=43)

3.4.3 Demographics of HCPs taking part in the concept mapping

The majority of the HCP group were doctors, including both hospital and general practitioners. Occupational therapists made up the next professional group in terms of numbers and nurses, psychologists, a podiatrist a physiotherapist and a service manager also took part. A breakdown of the professional groups within the HCP group can be seen in Figure 3:13.

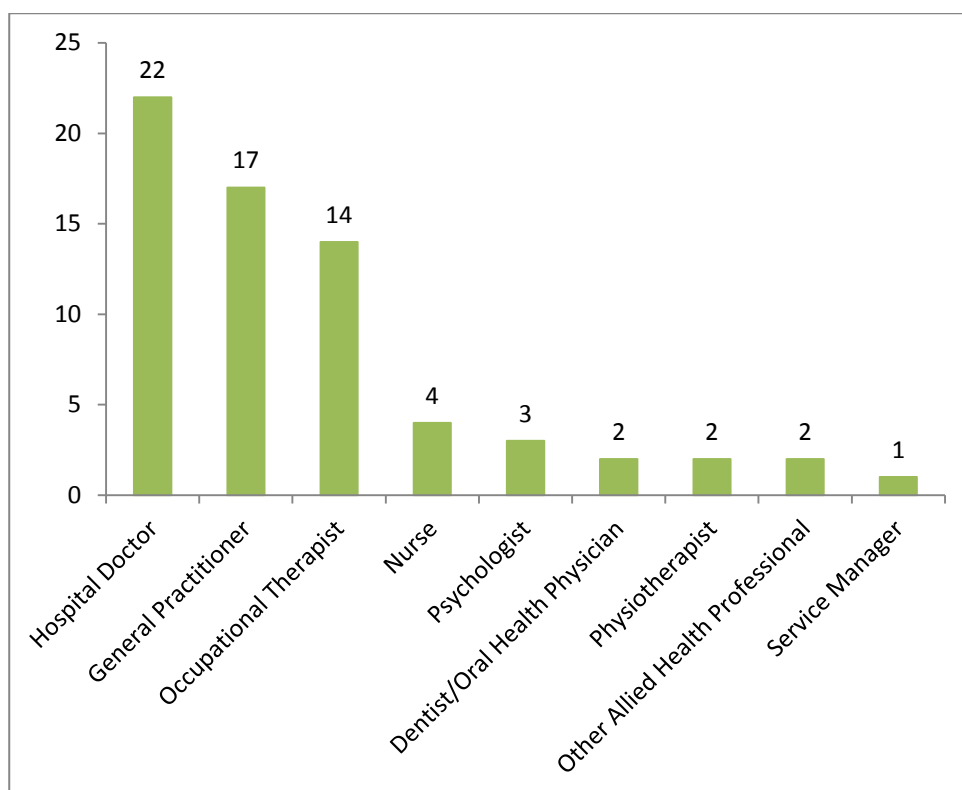


Figure 3:13 Professional groupings of the health care professional participants

3.4.4 Participation in each stage of GCM process

Overall, 232 participants took part in one or more stages of the GCM process.

Participation in the study has been broken down into participant group, stages of the concept mapping process and by participation type (online/postal or face-to-face). This breakdown can be viewed in Table 3-4.

Stage of concept mapping process	Patients with PSS	Adult house-hold members	Health care professionals	Total
Brainstorming	93	31	48	172
Sorting	61	22	46	129
Rating – Importance	91	31	59	181
Participation in any stage	121	43	67	232

Table 3-4 Number of participants in each stage of Concept mapping study by participant group

3.4.5 The statement reduction process

The brainstorming exercise generated 463 statements, which were subsequently distilled to a final set of 94 unique statements. A complete list of the numbered statements can be viewed in the Appendices (Section A.3).

3.4.6 Representing the ideas and initial interpretation: The concept maps

Multidimensional scaling resulted in a point map with a stress value of 0.18 (See Figure 3:14). Each numbered point within the map represents a statement.

Point Map

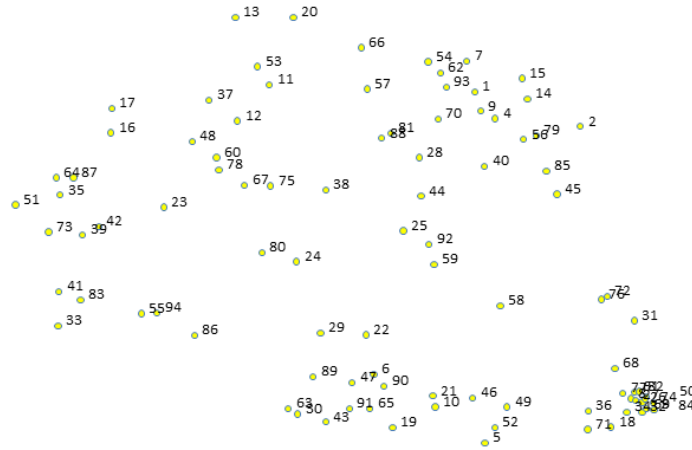


Figure 3:14 Point map depicting the numbered statements

Location and distance on the map have meaning: Statements which were frequently sorted together by participants are located close to each other on the map; statements which were rarely sorted into the same groups as each other are located further away from each other. Figure 3:15 demonstrates how statements, which are very differently to each other conceptually, are located some distance away from each other on the point map.

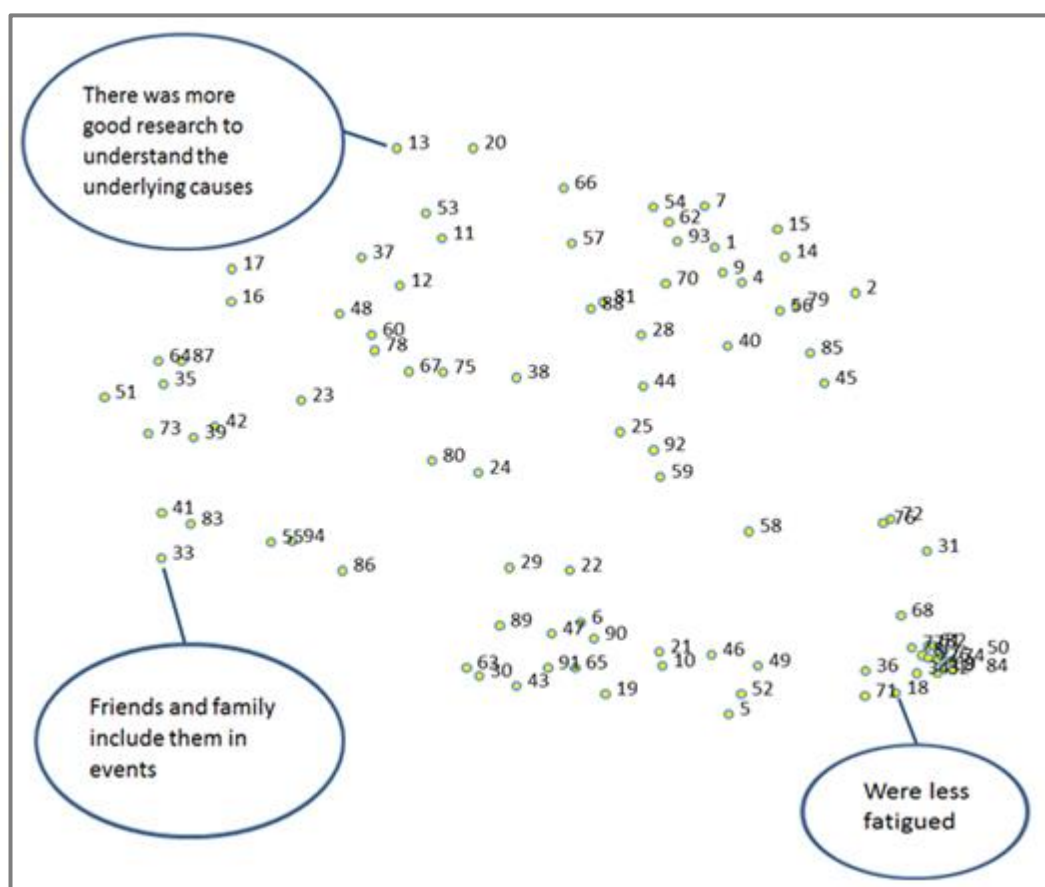


Figure 3:15 Point map demonstrating how statements which are very different conceptually, are distant from each other on the map

Conversely, Figure 3:16 shows how statements which are similar in meaning have ended up being in close proximity to each other on the map.

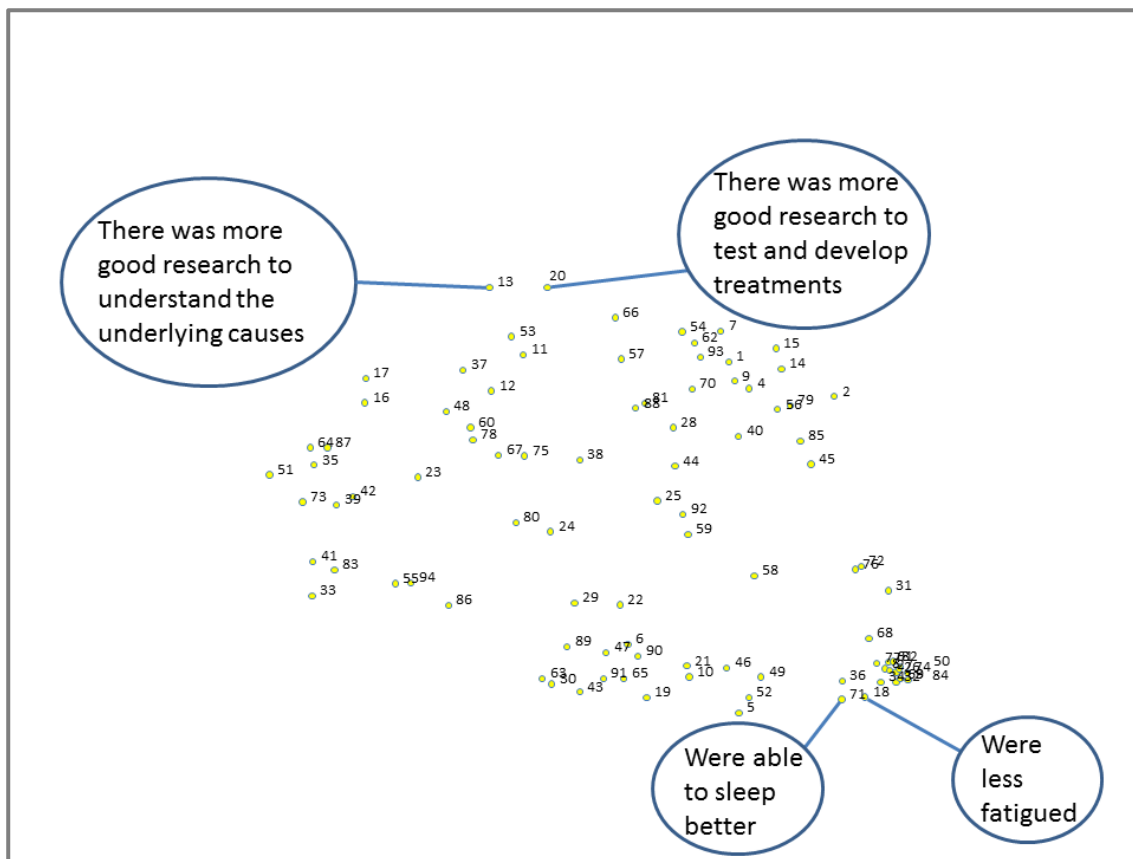


Figure 3:16 Point map demonstrating how statements similar in meaning are located near to each other on the map

3.4.6.1 Arriving at a cluster solution:

A 7-cluster solution was ultimately agreed upon. An example of an 8-cluster map is visible in (Figure 3:17). The next two clusters to be combined by Ward's algorithm are circled and labelled '*Mental wellbeing*' and '*Wellbeing*'. The statements within these two clusters are closely related conceptually to each other (see Table 3-5). It therefore made sense to combine them, creating one '*Wellbeing*' cluster.

8 Cluster Map

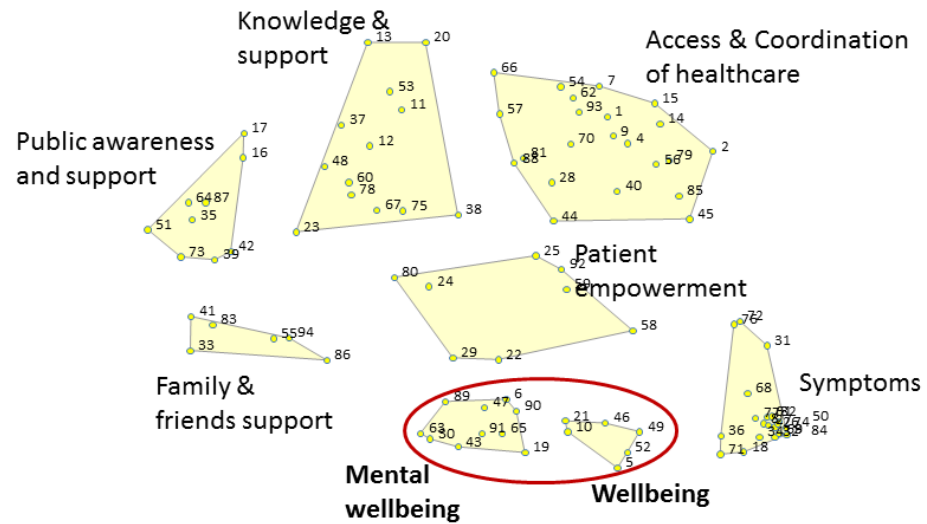


Figure 3:17 An 8 cluster map

Mental wellbeing cluster statements:	Wellbeing cluster statements:
6. They have a good diet	5. Could go out in the sun
19. Could come to terms with their symptoms	10. Were less stressed or worried
30 Could continue to drive	21. Feel in control of their symptoms
43. Have a positive attitude	46. They have better mobility
47. Exercise regularly	49. Could improve their concentration
63. Could come to terms with their limitations	52. Their mood was better
65. Learn to balance their activity and rest	
89. Develop good coping strategies	
90. Keep their body active	
92. Keep their mind active	

Table 3-5 Numbered statements within the two clusters which are next to merge

After these two clusters were combined to create the *'Wellbeing'* cluster, there were seven clusters. Following this iteration, the software next combined the *'Public awareness and support'* and the *'Family and friends support'* clusters to create six clusters. Although it made sense initially to combine these clusters, the statements within the *'Family and friends support'* cluster related much more to how someone with PSS might relate to others and how they might relate to them. The statements in the public awareness and support cluster conceptually related to how society could support them within the context of their disease. Therefore, a unanimous decision was made to keep these as two distinct clusters and choose a final seven cluster solution.

The seven cluster solution contained the following named clusters: (1) Access and coordination of healthcare; (2) Knowledge and support; (3) Public awareness and support; (4) Friends and family; (5) Symptoms; (6) Patient empowerment and (7) Wellbeing. The smallest cluster (Friends and family) contained 6 statements and the largest (Access and coordination of healthcare) 22 statements. The point cluster map

can be seen in Figure 3:18. Here each statement is again represented by a numbered point on the map and these points are grouped into the themed clusters.

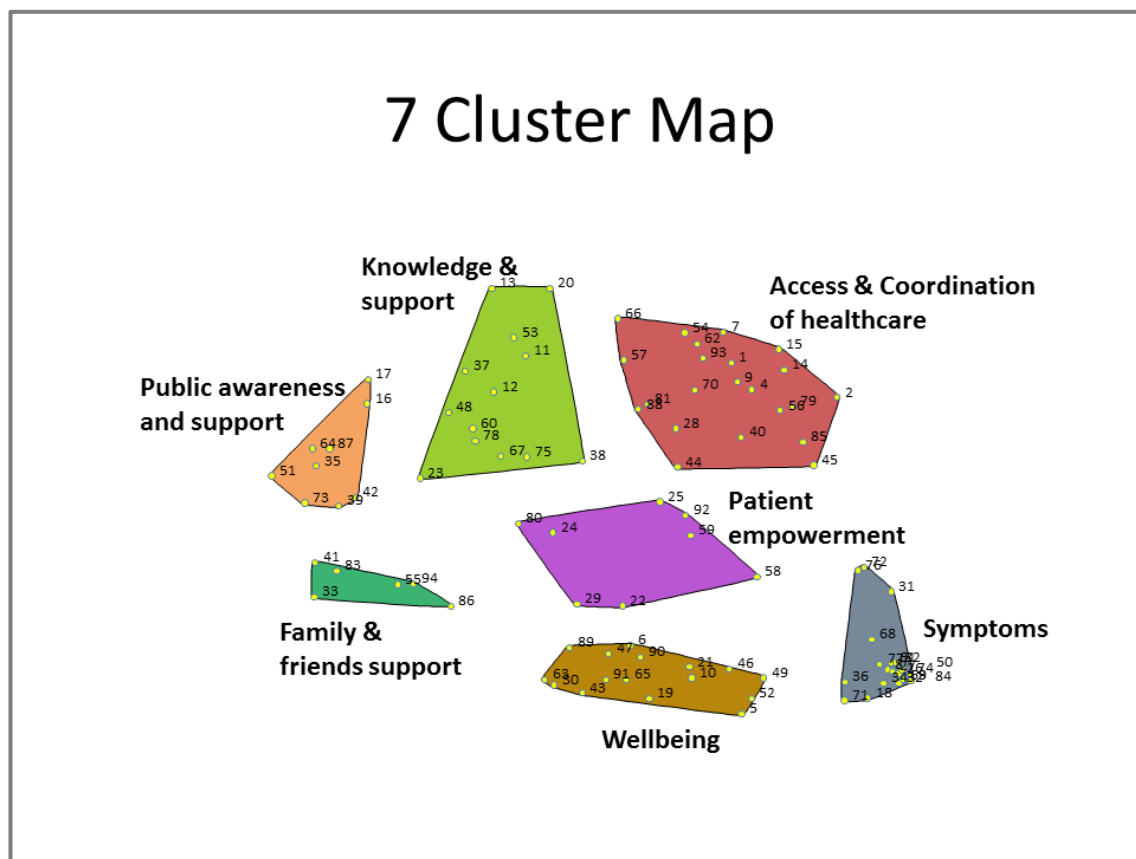


Figure 3:18 Point cluster map depicting the final 7 cluster solution

Average importance rating scores for each cluster for all stakeholder groups were next examined and can be seen in a cluster rating map (Figure 3:19). The clusters with the greater numbers of layers were rated as being of greater importance by participants. As can be seen within Figure 3:19, the statements falling within the Patient Empowerment cluster received the highest priority ratings out of a possible 5 (mean of 4.07) followed by the Symptoms cluster (mean of 3.98). The lowest rated cluster was Public Awareness and Support which had a mean rating score of 3.48.

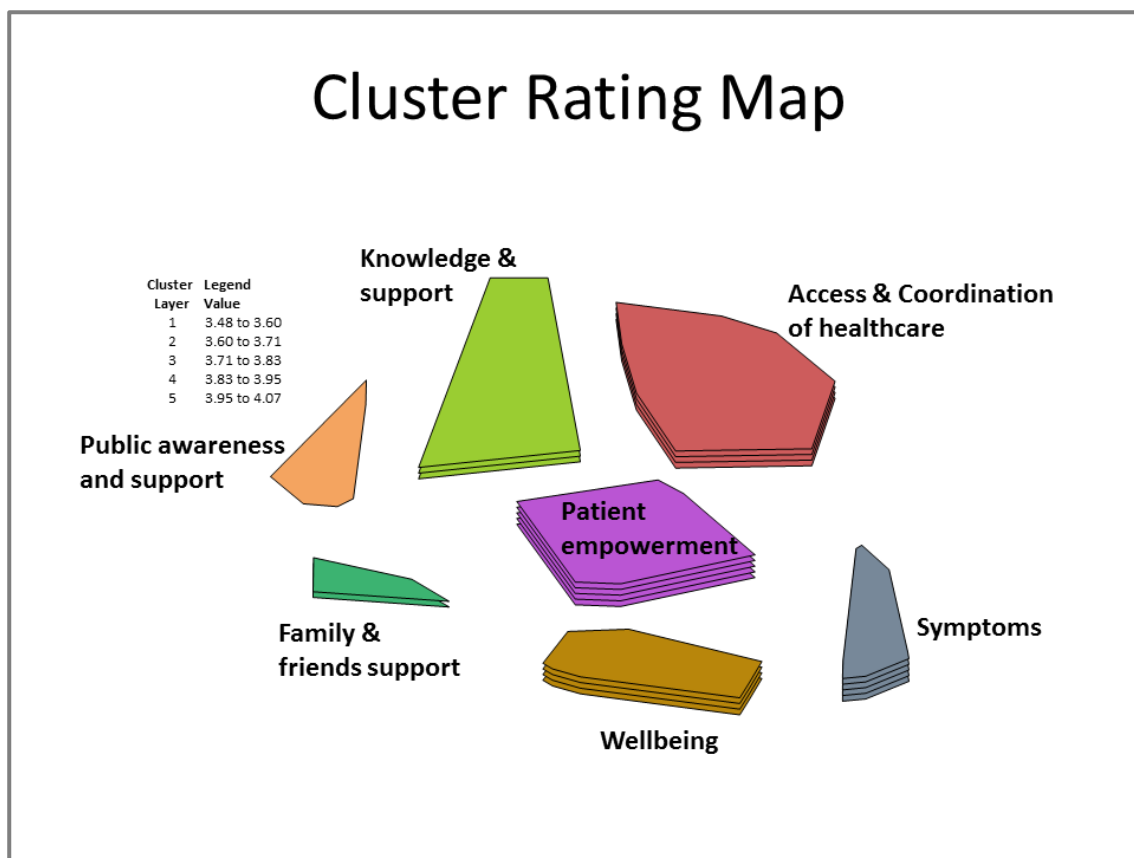


Figure 3:19 Cluster rating map

To determine if there were any differences between the three stakeholder groups' importance ratings for the different clusters, a 'pattern match' was generated (see Figure 3:20). This demonstrated a high level of agreement between participant groups for the importance ratings for each cluster. PSS patients and AHMs both viewed Patient Empowerment and Symptoms as being the most important concepts. HCPs viewed Patient Empowerment and Wellbeing as being the most important, followed by symptoms. All groups agreed that Public Awareness and Support was the least important concept in the context of people with PSS being able to do everyday activities of their choosing.

Pattern Match

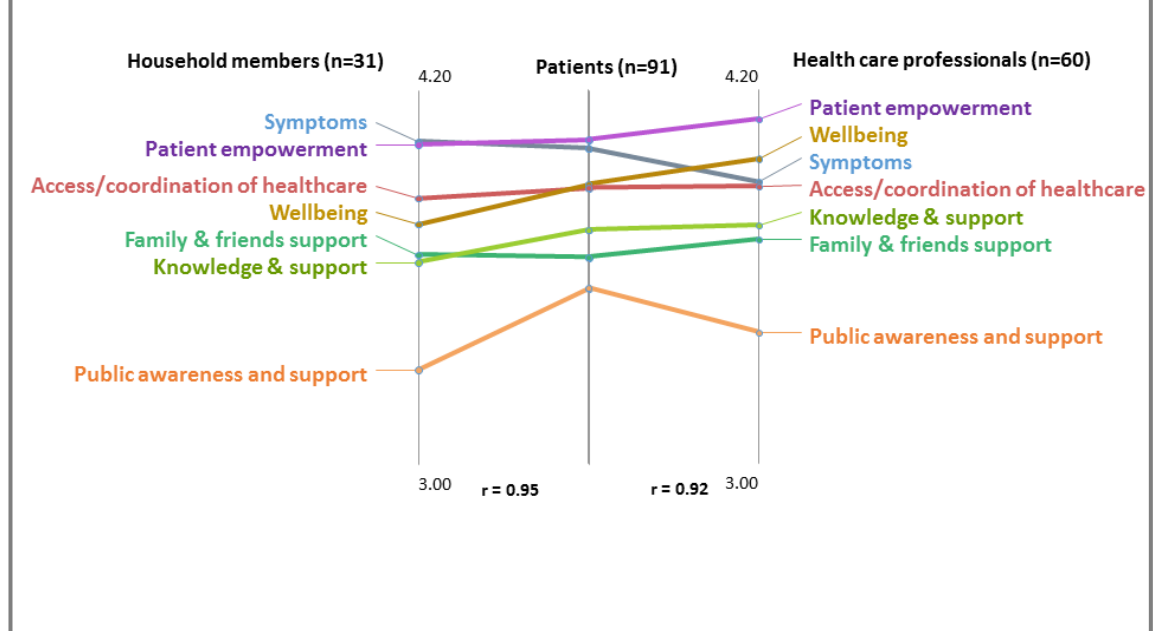


Figure 3:20 Pattern match demonstrating importance ratings for each cluster by participant group

‘Go-zones’ or bivariate plots of importance ratings for all statements were next examined for two participant groups at a time (see Figure 3:21). There was a higher correlation between rating data for the PSS and AHM group ($r=0.89$) compared with the PSS and HCP groups ($r=0.68$) and HCP and AHM groups ($r=0.73$). Therefore to examine the priority statements within each cluster, the PSS and AHM groups were combined. This meant the importance ratings were compared with the ‘lived experience’ group (PSS and AHM groups combined) and the HCP group. The similarities and differences were examined in go-zones which were generated for each of the clusters. Each cluster is discussed in turn, in decreasing order of importance as ranked by participants.

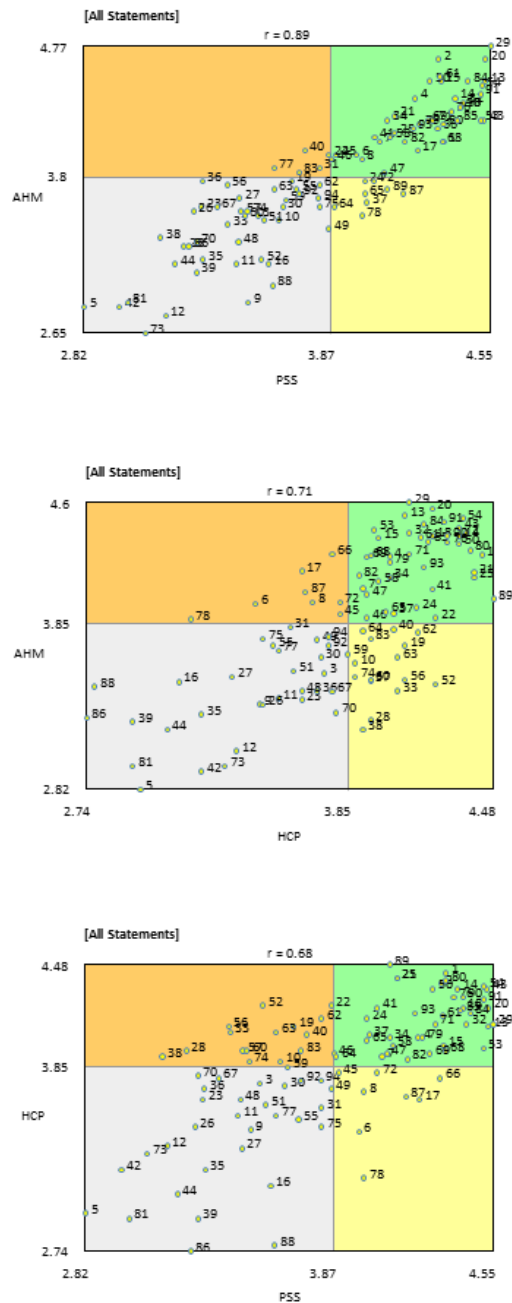


Figure 3:21 Go zones showing importance ratings for all statements comparing each of the participant groups

Cluster 1: Patient empowerment

Participants who took part in the rating exercise rated Patient empowerment as the most important cluster. This cluster contains 8 statements. Table 3-6 shows the mean importance ratings given by all participants for each of the statements. Within the cluster statement #29 *'There was a cure'* was seen as the most important followed by #80 *'Felt they were being taken seriously'* and #25 *'Have support to manage their symptoms themselves'*.

Statements		Mean Importance Rating
29	There was a cure	4.45
80	Felt they were being taken seriously	4.34
25	Have support to manage their symptoms themselves	4.22
58	Take their medication as prescribed	4.07
24	Have confidence to seek advice when needed	4.02
22	Look after their physical, emotional and spiritual wellbeing	4.00
92	Were taught relaxation techniques	3.74
59	Have support with memory and concentration difficulties	3.73

Cluster importance rating mean = 4.07 (SD 0.24)

Table 3-6 Patient empowerment cluster: Statements and importance ratings

In order to identify any differences in opinion between participant groups for the importance of each statement within this cluster, a go zone (explained earlier in Section 3.2.2) was created (see Figure 3:22). Here I made a comparison between two groups; those with the 'lived experience' of PSS (PSS patients and AHMs) and HCPs. The go zone has identified that the top three priority statements within the green zone are the same as those identified in Table 3-6. Similarly, the least priority statements within the table were those identified by both participant groups as being the least important (#92 *'Were taught relaxation techniques'* and #59 *'Have support with memory and concentration difficulties'*).

HCPs perceived that if people with PSS were able to look after themselves well (#22 *'Look after their physical, emotional and spiritual wellbeing'*) and have the confidence

to seek appropriate advice when required, they would be able to do more day-to-day activities of their choosing.

PSS patients and AHMs perceived that it was important to '*Take their medication as prescribed*' (#58). However, these statements were very near the cut off for the green go-zone areas and although they have highlighted some slight differences between the two groups, they were still rated at ≥ 4 out of 5 overall for all groups combined (see Table 3-6).

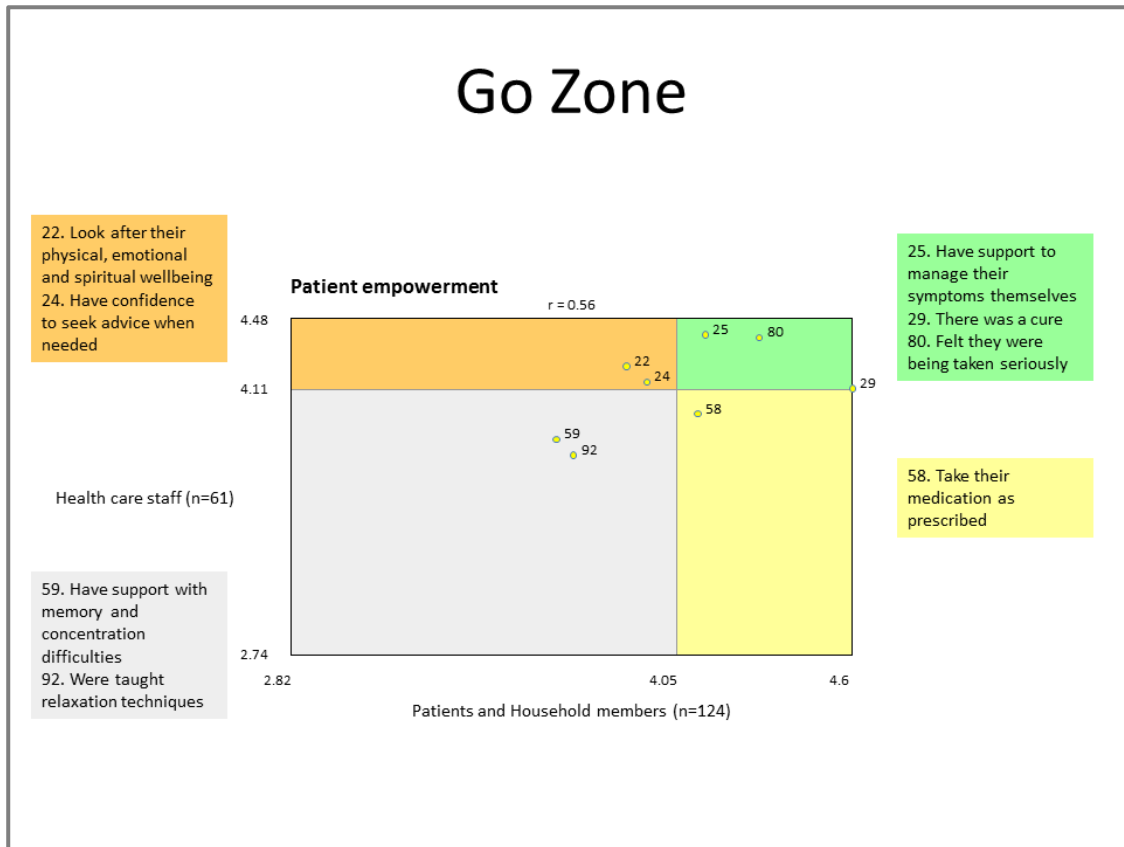


Figure 3:22 Go zone identifying importance of each statement within the Patient Empowerment cluster

Cluster 2: Symptoms

The next most important cluster was the Symptoms cluster. This cluster contains 20 statements which all relate to symptoms of PSS. Table 3-7 shows the mean importance ratings given by all participants for each of the statements. Statements relating to ocular dryness, pain and fatigue were rated as being the most important with skin and vaginal dryness being rated as the least important.

Statements		Mean Importance Rating
84	Their eyes were less dry	4.37
50	Have less pain	4.34
18	Were less fatigued	4.34
76	Fatigue was better managed/treated	4.34
32	Their vision was not impaired	4.32
61	Their eyes were more comfortable	4.31
71	Were able to sleep better	4.23
68	Have healthy teeth and/or comfortable dentures	4.17
69	Their throat was less dry	4.16
34	Swallowing was easier	4.10
82	Mouth and lips were less dry	4.07
72	Gastrointestinal (stomach and bowel) problems were managed	3.93
8	Were less prone to getting infections	3.89
31	Skin problems were treated	3.76
74	Were less breathless	3.64
77	Have more feeling in their mouth and lips	3.64
3	Did not have mouth sores or ulcers	3.61
36	Didn't have sexual problems	3.54
27	Their skin was less dry	3.46
26	Their vagina was less dry	3.40

Cluster importance rating mean = 3.98 (SD 0.33)

Table 3-7 Symptoms cluster: Statements and importance ratings

In order to identify any differences in opinion between participant groups for the importance of each statement within this cluster, a go zone was created (see Figure 3:23). This identified that symptoms relating to fatigue, pain, sleep and oral and ocular dryness were considered as being of highest importance. The ten statements within

the green go zone area were the same statements which were identified as being the most important in Table 3-7.

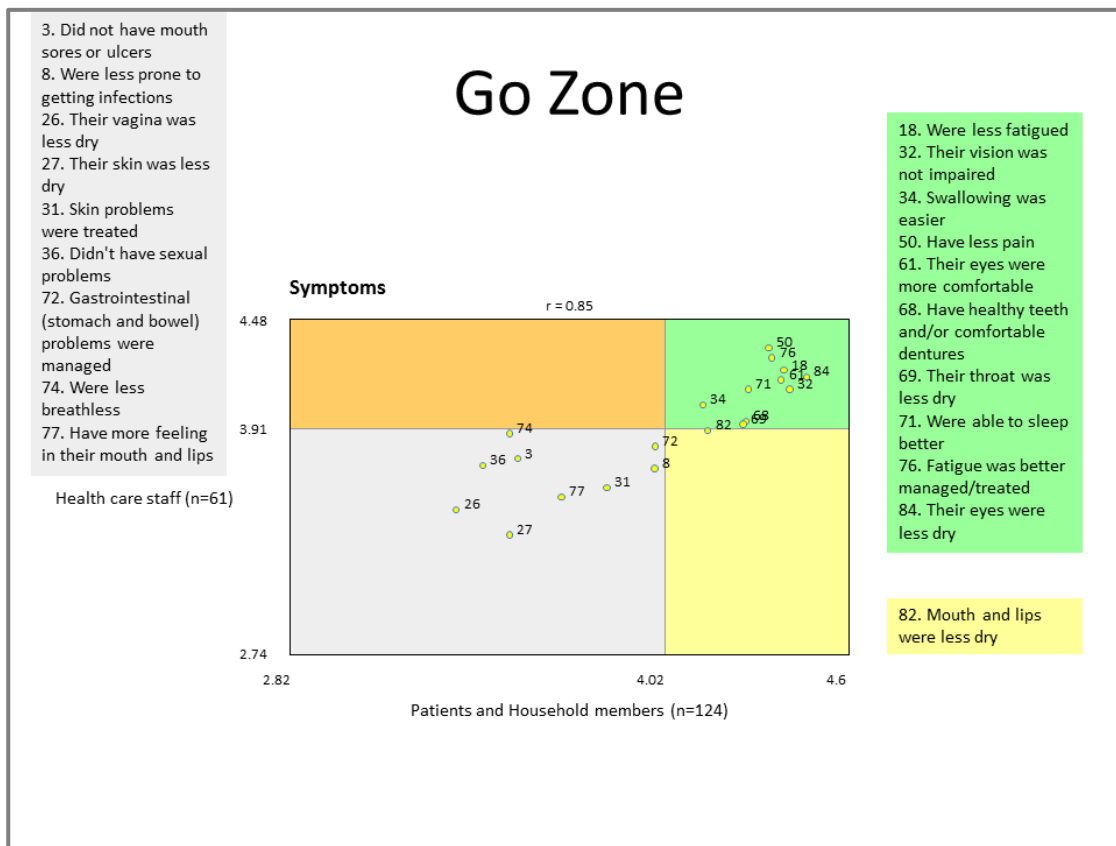


Figure 3:23 Go zone identifying importance of each statement within the Symptoms cluster

Cluster 3: Wellbeing

The cluster, which was the third highest rated cluster to emerge from the concept mapping process, was the Wellbeing cluster. This cluster contains 16 statements. Table 3-8 shows the mean importance ratings given by all participants for each of the statements.

Statements		Mean Importance Rating
91	Keep their mind active	4.41
43	Have a positive attitude	4.41
90	Keep their body active	4.36
21	Feel in control of their symptoms	4.24
89	Develop good coping strategies	4.17
47	Exercise regularly	4.01
65	Learn to balance their activity and rest	3.96
46	They have better mobility	3.90
19	Could come to terms with their symptoms	3.84
6	They have a good diet	3.79
63	Could come to terms with their limitations	3.78
49	Could improve their concentration	3.75
52	Their mood was better	3.73
10	Were less stressed or worried	3.69
30	Could continue to drive	3.68
5	Could go out in the sun	2.86

Cluster importance rating mean = 3.91 (SD 0.38)

Table 3-8 Wellbeing cluster: Statements and importance ratings

A go zone was created to identify the statements falling in the green priority area (see Figure 3:24). The top five statements within Table 3-8, all fell within the green area of the go zone. The HCP group saw certain statements as priorities. These include statements #19 *'Could come to terms with their symptoms'*, #63 *'Could come to terms with their limitations'* and #52 *'Their mood was better'*. From the HCP group perspective, acceptance of the disease and its limitations and an improvement in mood could potentially result in people with PSS being able to carry out more daily activities of their choosing. Those in the lived experience group perceived that a good diet, better mobility and regular exercise could help a person with PSS to do more daily

activities. Both groups compared within the go zone identified that going out in the sun (#5) was a very low priority in comparison to the other statements.

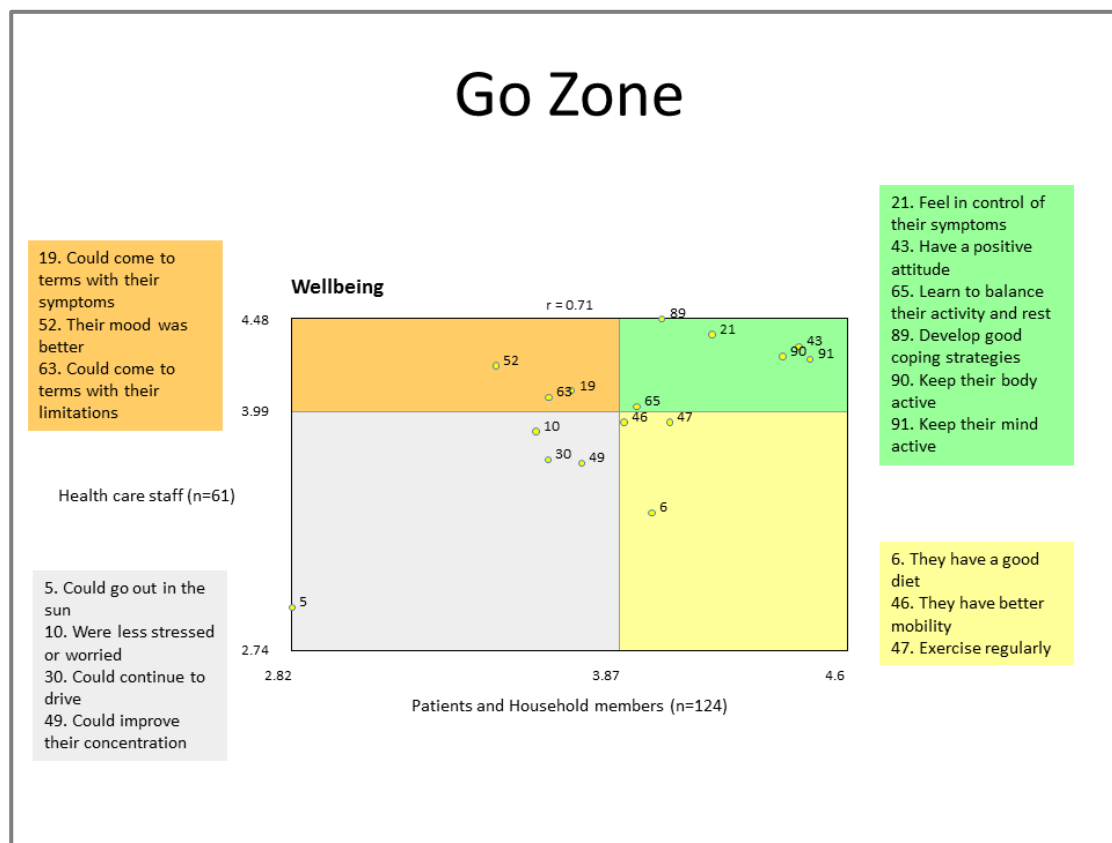


Figure 3:24 Go zone identifying importance of each statement within the Wellbeing cluster

Cluster 4: Access and coordination of healthcare

This cluster contained 22 statements. Statement #54 'There is good communication between clinicians' was rated as the most important within this cluster (See Table 3-9). Other priority statements related to accessing good drug treatments and knowing who to contact when symptoms flared up and also having access to professional support during a flare. Statements relating to access to specific types of therapies were seen as lower priorities.

A go zone was also created for this cluster (see Figure 3:25). The important statements within Table 3-9 can be seen within the green area of the go zone. HCPs rated some statements relating to specific things that health care professionals could do for their patients as being important. These include providing individualised treatment plans, signposting to appropriate support groups and charities and raising sensitive topics in

consultations. They also saw access to psychological support and a specialist nurse as being a priority. The PSS patients and AHMs did not see these as priorities.

Statements		Mean Importance Rating
54	There is good communication between clinicians	4.45
2	Have access to a range of good drug treatments	4.39
14	Have professional support during a flare up of symptoms	4.37
1	Know who to contact when their symptoms flare up	4.32
85	Associated conditions are diagnosed and treated	4.31
15	Can see a consultant when needed	4.25
93	Their healthcare is better coordinated	4.20
4	Knew the range of available treatment options	4.18
79	Diagnosis was quick	4.17
66	There was more funding for specialist rheumatology services	4.12
7	There were "one stop" Sjögren's clinics with all relevant health care professionals available	4.02
62	Have access to a specialist nurse	3.91
40	Have an individualised treatment plan	3.90
45	There was better management of the side effects of drugs	3.88
56	Health care professionals would raise sensitive topics (e.g. sex and vaginal dryness) during consultations	3.71
57	Professionals could direct them to support groups and charities	3.66
28	Have access to psychological support	3.49
70	Have access to occupational therapy	3.46
9	Have access to physiotherapy	3.39
88	Have access to complementary therapies or alternative remedies	3.23
44	There were diaries for recording symptoms and problems to bring to appointments with health care professionals	3.16
81	Have access to hydrotherapy	2.96

Cluster importance rating mean = 3.89 (SD 0.43)

Table 3-9 Access and coordination of healthcare cluster: Statements and importance ratings

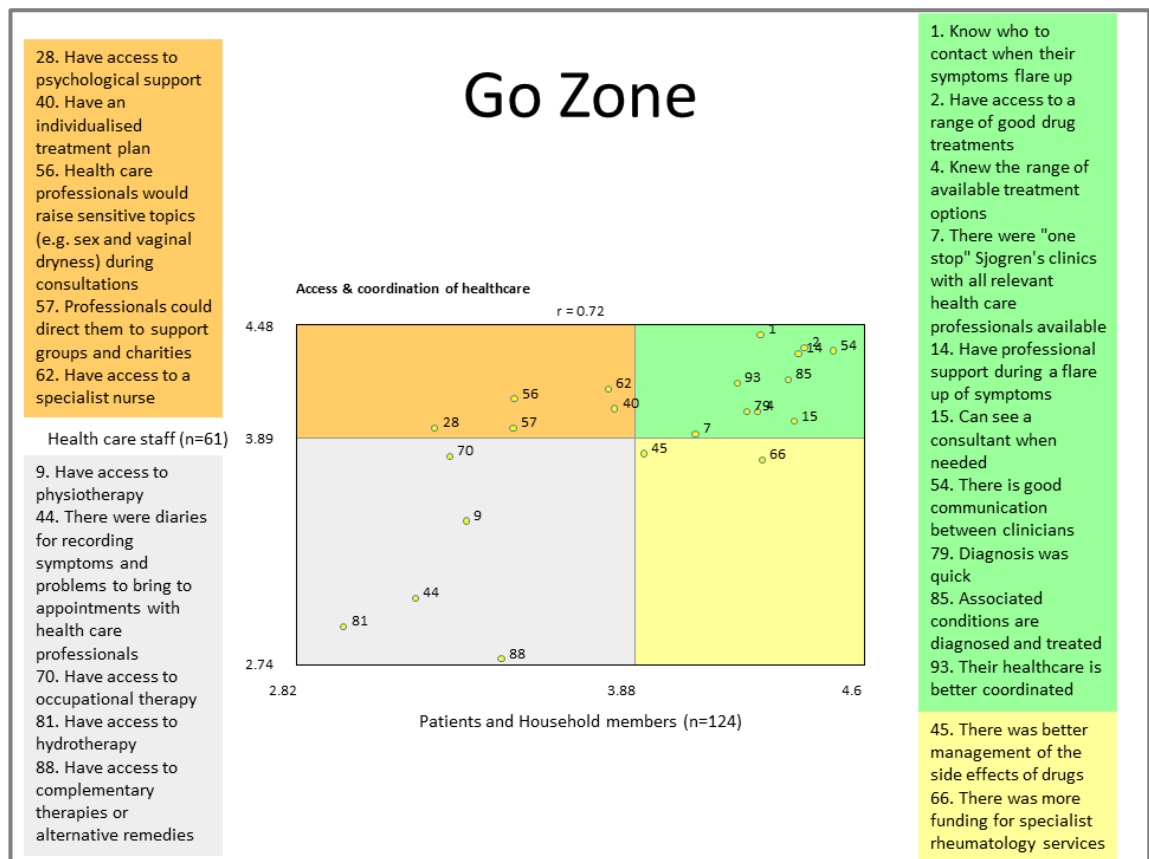


Figure 3:25 Go zone identifying importance of each statement within the Access & coordination of healthcare cluster

Cluster 5: Knowledge and support

As can be seen in Table 3-10, the Knowledge and support cluster contained 13 statements. The most important statements were those which related to the need for more research to develop and test treatments and research to understand the causes of the disease. This was closely followed by statements relating to education on PSS for both healthcare professionals and patients. The lowest priority statement was about there being appropriate aids and adaptations in the community.

Statements		Mean Importance Rating
20	There was more good research to test and develop treatments	4.45
13	There was more good research to understand the underlying causes	4.38
53	There was education on Sjogren's for healthcare professionals	4.28
37	There was education on Sjogren's for patients	3.97
75	There was information available on exercise and Sjogren's	3.67
60	Have access to support and advice from other people with Sjogren's	3.66
78	Have help with dental costs	3.65
67	Felt a family member or supporter would be welcome at their appointments	3.55
48	Have access to appropriate aids and adaptations in their homes	3.51
23	Felt a family member or supporter could be included in their care planning	3.48
11	Have Sjogren's advice leaflets	3.44
38	Could access support to help set personal goals	3.44
12	There were appropriate aids and adaptations in the community	3.17

Cluster importance rating mean = 3.74 (SD 0.39)

Table 3-10 Knowledge and support cluster: Statements and importance ratings

The go zone for this cluster (Figure 3:26) confirms that both groups considered the statements on research and education to be of most importance. Compared to other clusters, there was a lower level of agreement between the two groups ($r=0.54$). This reflected a difference in priorities for some of the statements between the HCPs and those with the lived experience of PSS. The PSS group considered having help with dental costs and having information on exercise as being a priority relative to other statements within the cluster, but these were seen as less important by HCPs. However, the HCP rated more highly statements around having support to set personal goals, welcoming family members to appointments and having access and support from others with the disease. Both groups considered having aids and adaptations in the community a lower priority.

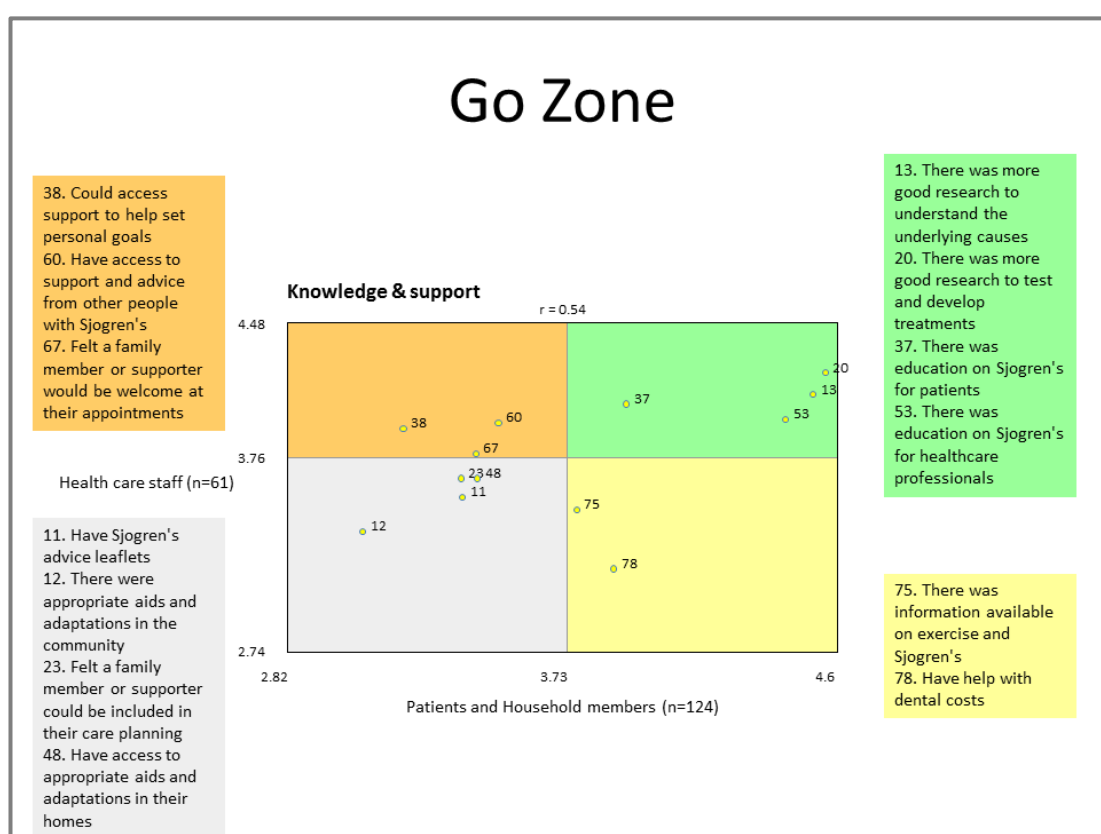


Figure 3:26 Go zone identifying importance of each statement within the Knowledge & support cluster

Cluster 6: Friends and family

The Friends and family cluster was rated as the second least important cluster and contained 6 statements which can be viewed in Table 3-11. The most important

statement was #41 *'Have supportive family and friends'*. The least important statement was #86 *'On a bad day people could tell by looking at them how they are feeling'*. Compared to other clusters, there was a lower level of agreement between the two groups ($r=0.54$). This reflected a difference in priorities for some of the statements between the HCPs and those with the lived experience of PSS. The lived experience group considered being able to describe PSS to others as being a priority relative to other statements within the cluster, but was not considered as being as important by HCPs. However, the HCP rated more highly - in relation to other statements in the cluster – the inclusion of people with PSS in events by their friends and family.

Statements		Mean Importance Rating
41	Have supportive family and friends	4.12
83	Family could understand the symptoms	3.83
94	Can explain to others what they can and cannot do	3.78
55	Could easily describe Sjogren's to others	3.66
33	Friends and family include them in events	3.65
86	On a bad day people could tell by looking at them how they are feeling	3.10

Cluster importance rating mean = 3.69 (SD 0.30)

Table 3-11 Friends and family cluster: Statements and importance ratings

The go zone for this cluster (Figure 3:27) confirmed that both groups considered having supportive friends and family as being of most importance in this cluster. Both groups also agreed that the lowest priority statement was about others being able to know how a person with PSS was feeling on a bad day. However, both groups considered being able to explain to others about their disease and having family who understood the symptoms as being important.

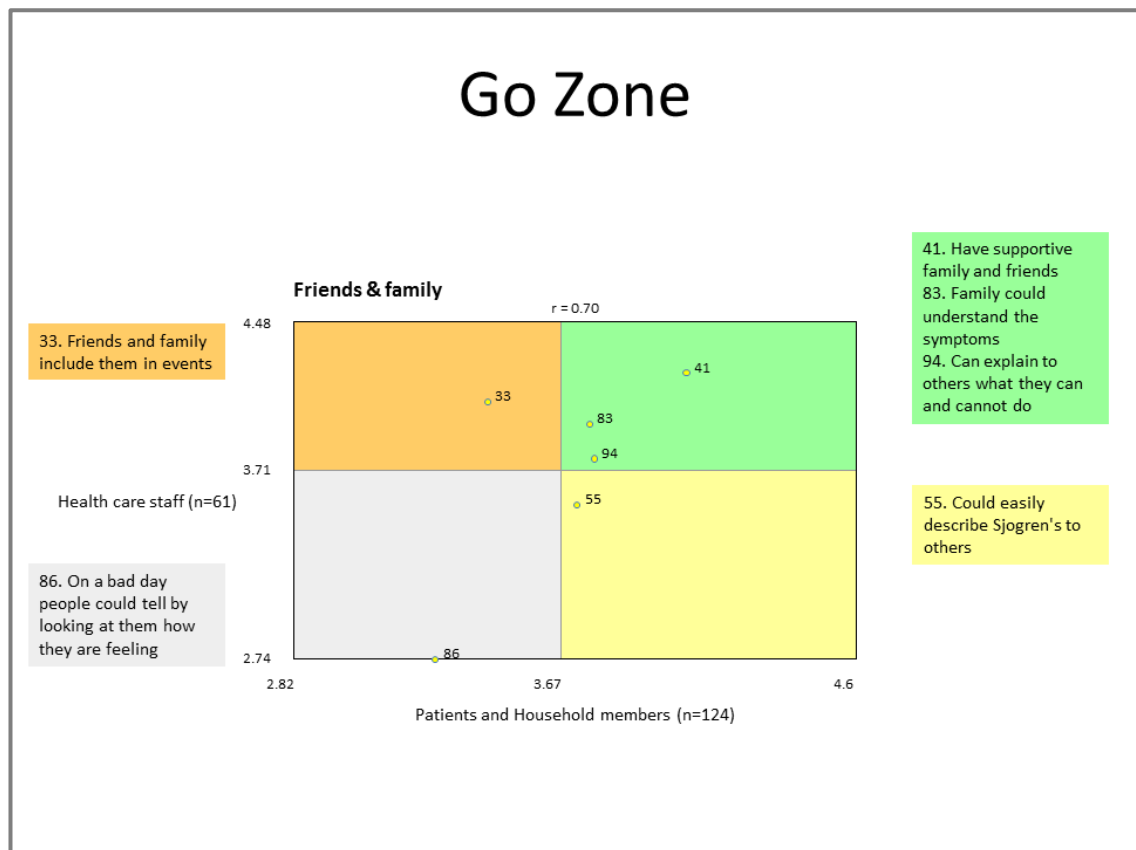


Figure 3:27 Go zone identifying importance of each statement within the Friends and family cluster

Cluster 7: Public awareness and support

The Public awareness and support cluster was rated as the least important cluster. There were 9 statements in this cluster (see Table 3-12). Priority statements for this cluster relate to education for people who fund services and being eligible for benefits if unable to work. Statements which were regarded as less important were #42 'Have assistance with shopping, cleaning etc.' and #73 'Public transport was accessible'.

Statements		Mean Importance Rating
17	There was education about Sjogren's for people who fund services	4.01
87	Those unable to work and/or needed support to function, were eligible for benefits	3.92
64	Employers were aware of things they could do in the workplace that are helpful for people with Sjogren's	3.85
51	There was education on Sjogren's for family members	3.59
16	There was education about Sjogren's for the general public	3.38
35	Public spaces were more Sjogren's friendly e.g. heated/lit/airconditioned differently	3.28
39	Have a disabled parking badge	3.14
73	Public transport was accessible	3.09
42	Have assistance with shopping, cleaning etc.	3.04

Cluster importance rating mean = 3.48 (SD 0.36)

Table 3-12 Public awareness and support cluster: Statements and importance ratings

The go zone for this cluster (see Figure 3:28) showed that both groups agreed about priorities within this cluster and agreed about what was less important. Examples of priorities included education for those who fund services for PSS patients and for family members, benefits for people with PSS who are unable to function well or work, and awareness of employers to make appropriate adjustments within the workplace for employees with PSS. Lower priorities included accessible public transport, lighting and air-conditioning within public spaces, domestic support, and education about PSS for the general public.

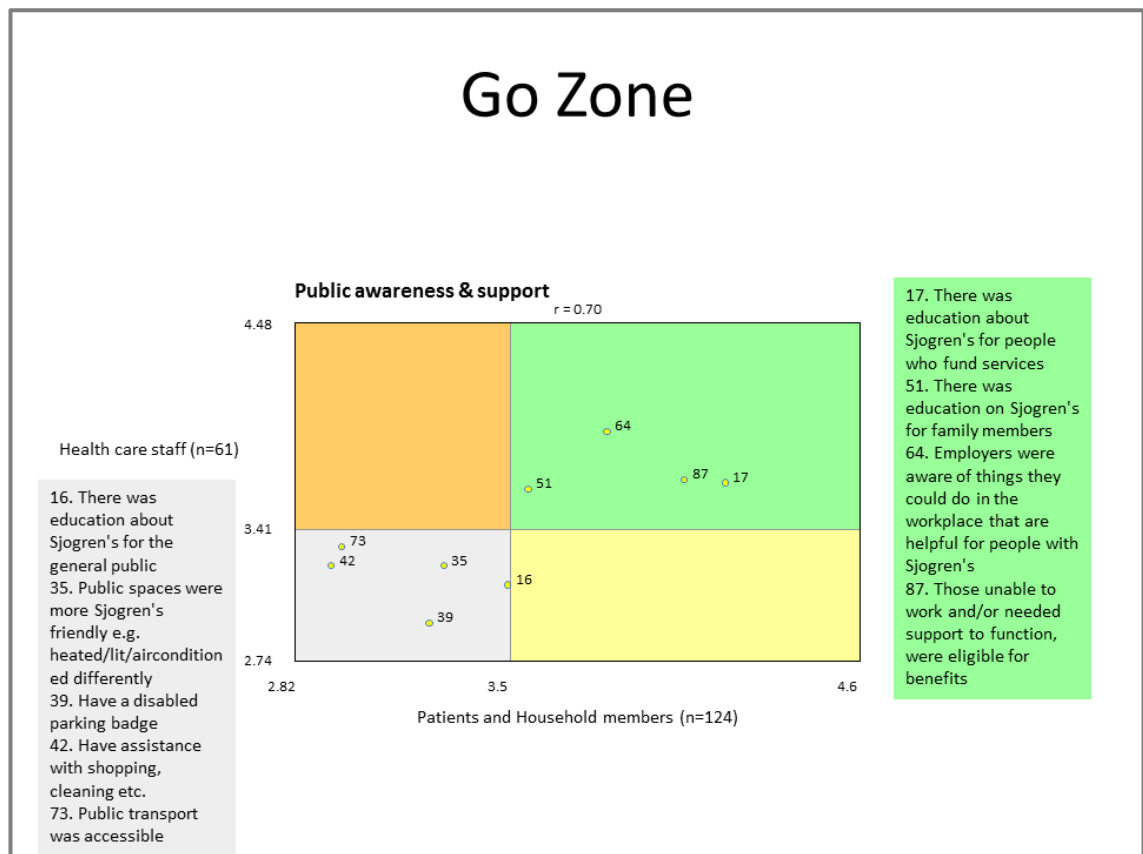


Figure 3:28 Go zone identifying importance of each statement within the Public awareness and support cluster

3.5 Discussion

This concept mapping study has highlighted that PSS patients, AHMs and HCPs consider that in the context of people with PSS being able to participate more and carry out day-to-day activities of their choosing, the concepts of '*Patient empowerment*' and managing '*Symptoms*' are particularly important.

3.5.1 Discussion of demographic results

The PSS participants who took part in this exercise had a mean age of 63 years, which is similar to the average age in a study which included the majority of the UKPSSR cohort (mean of 61 years) (Lendrem *et al.*, 2014). The average number of years since diagnosis in this study was 10. It is therefore possible that newly diagnosed patients and their family members may have given different responses to those in this study. In order to investigate this further, I conducted a subgroup analysis by creating a pattern match to compare the mean importance rating values at cluster level from those who

had a diagnosis of PSS (PSS patients and AHMs) of ≤ 5 years ($n=34$) and those who had a PSS diagnosis for >5 years ($n=88$). This revealed a high level of agreement ($r=0.96$). This result indicates that length of disease does not seem to influence how those with a lived experience of PSS prioritise the identified themes. However, it is still conceivable that 'newly' diagnosed PSS patients may have different needs and a separate study focussing on this subgroup of patients is needed to address this.

13% of the PSS patients who took part in this study were male, which is slightly greater than the proportion of males (9%) reported in a recent meta-analysis of PSS studies which included 7888 participants (Singh *et al.*, 2016). As the proportion of males in this study was greater than the proportion of males represented in other PSS studies, I compared the differences in importance ratings at cluster level between males and female PSS participants (males, $n=10$, females, $n=83$) by creating a pattern match. This revealed no differences in importance ratings between males and females ($r=0.99$). Therefore, despite a relatively greater proportion of male PSS patients taking part in this study, there was a very high level of agreement between males and females and the increased male representation did not influence the overall priority scores.

The SF-36 norm-based scores for the PSS patients indicated that their quality of life was significantly reduced compared to the US norm scores. This is clinically as well as statistically significant as a difference of 3-5 below 50 is regarded as clinically significant (Saris-Baglama *et al.*, 2011). PSS participants in particular had low mean norm-based physical component summary scores (38.15 SD 11.03). Low scores in domains which relate to activities of daily living and participation (Physical Functioning, Role Physical, Social Functioning and Role Emotional) further add to the body of literature (Hackett *et al.*, 2012a; Hackett *et al.*, 2012b), which proposes and demonstrates that people with PSS have difficulties performing daily activities and taking on life roles.

Conversely, the AHM group had significantly better quality of life as measured by the SF-36 compared with the US norm scores for the Mental Health and Social Functioning domains. However, the low t-values for these domain scores indicates that the differences were minimal. Furthermore, the smaller AHM cohort, may not have been sufficiently powered and there may be differences in scores between people in the US

and those in England. To my knowledge, quality of life scores in family members of people with PSS have not previously been reported.

Caregiver strain was present in 14% of AHMs and as would be expected, this is lower than CSI scores reported for those living with someone who had recently had a stroke (Blake *et al.*, 2003), traumatic brain injury (Fortune *et al.*, 2016) or recently discharged from a critical care unit (McPeake *et al.*, 2016). However, the level of carer strain in adults living with someone with PSS, was similar to the levels reported by carers who live with someone who has Parkinson's disease (Wade *et al.*, 2003). Carer strain could be evident in AHMs living with someone who has PSS and clinicians should be aware of this possibility.

3.5.2 Discussion of concept mapping results

The point map had a stress value of 0.18. In multi-dimensional scaling, lower stress values are preferred as they reflect a better goodness of fit of the final point map representation with the original inputted similarity matrix (Kruskal, 1964; Rosas and Kane, 2012). Stress values for concept mapping studies should ideally fall below 0.39 (Trochim, 1989) and a recent pooled concept mapping study analysis of 69 studies demonstrated an average stress value of 0.28 (SD = 0.04, range: 0.17–0.34, 95% CI [0.27, 0.29]) (Rosas and Kane, 2012).

In general, this study has shown that HCP, PSS patients and AHM have similar priorities. However, there are some subtle differences and these were identified in the pattern match and the go zones. The main priority identified in this study by all stakeholder groups, was the need for patient empowerment. Patients can be further empowered by being key contributors in the design of services and symptom management programmes.

3.6 Conclusions

In order for people with PSS to improve their functional capacity and ability to participate in valued life activities, it is a priority that they are empowered and given support to manage their symptoms and improve their wellbeing. There was a high level of agreement between the participant groups regarding these priorities.

3.7 Summary

In this chapter, I have reported the methods and results of a concept mapping study involving 232 participants. The participants included a range of health care professionals representing different professional groups from across the UK and PSS patients and adult household members from different sites across England. This is a large-scale concept mapping study and the results are likely to be representative of UK PSS patients and clinicians who treat them. In the following chapter, I discuss the concept maps further and I present a summary report resulting from the interpretation sessions of the concept mapping data, which took place with my study advisory group.

Chapter 4. Intervention planning: Utilising the concept mapping results

In the previous chapter, I reported the methods and results of a group concept mapping study involving 232 participants from three stakeholder groups. In this chapter, I discuss these results further and describe some group interpretation discussions held with members of the study advisory group. The purpose of these interpretation sessions was to identify future intervention targets and facilitators from the concept mapping data. I discussed these targets with clinical members of the study advisory group and some other experienced clinicians. I asked them to consider a number of priority statements from the concept map in turn and comment on whether it could be an intervention, an outcome or both. I also asked them to provide specific examples. I collated the responses to form the basis of a focus group outline plan for discussion with PSS patients and AHMs.

4.1 Background

In the previous chapter, I asked three stakeholder groups to identify factors (in the form of statements) preventing or facilitating people with PSS from being able to participate and perform daily activities. Participants ordered these statements into themes (or clusters) and ranked them for importance and the results can be seen in Chapter 3. Interpretation of these results is key and the final part of the concept mapping process (see 3.2.3). The results and interpretations from this broad stakeholder engagement concept mapping process and the appropriate subsequent interpretations can be reported back to stakeholders and used to guide future planning (Trochim *et al.*, 2004).

The reason for making further interpretations to the concept mapping results was to determine i) the general themes and ii) the specific ideas from within the concept maps which will form both priority intervention target areas and specific components of a future intervention package. These interpretations will guide future non-pharmacological interventions to support patients with PSS to improve participation and ability to perform their daily activities.

In GCM studies with large numbers of stakeholders, it is common for key study group members to have made some interpretations to the concept maps prior to presenting the results and interpretations back to other stakeholders (Kane and Trochim, 2007). Furthermore, some of the priority statements within the concept maps, identified by key stakeholders (in Chapter 3), might be regarded as either potential intervention components, outcome measures, or both. In this chapter, members of the study advisory group and clinicians specialising in the intervention target areas identify possible intervention components and outcomes from the concept maps. By highlighting the prioritised needs of the community and then further involving those who are likely to be part of the intervention delivery process, it maximises the potential implementation success of a future intervention package (Kelly *et al.*, 2007). The initial interpretation of the concept mapping results produced in the previous chapter (Chapter 3) is used as a starting point in the utilisation of the concept mapping results as part of an intervention development process.

4.2 Aims of chapter

- To identify priority target areas from within the concept maps for future patient non-pharmacological interventions to improve participation and ability to perform daily activities for people with PSS.
- To identify specific intervention components from within the concept maps which might form part of a future intervention package.
- To provide a discussion framework for future focus group meetings with PSS patients and AHMs to discuss the intervention target areas and potential intervention components.

4.3 Method

The flow chart (Figure 4:1) gives an overview of the process which took place resulting in specific priority intervention targets and identified intervention components and possible outcome measures.

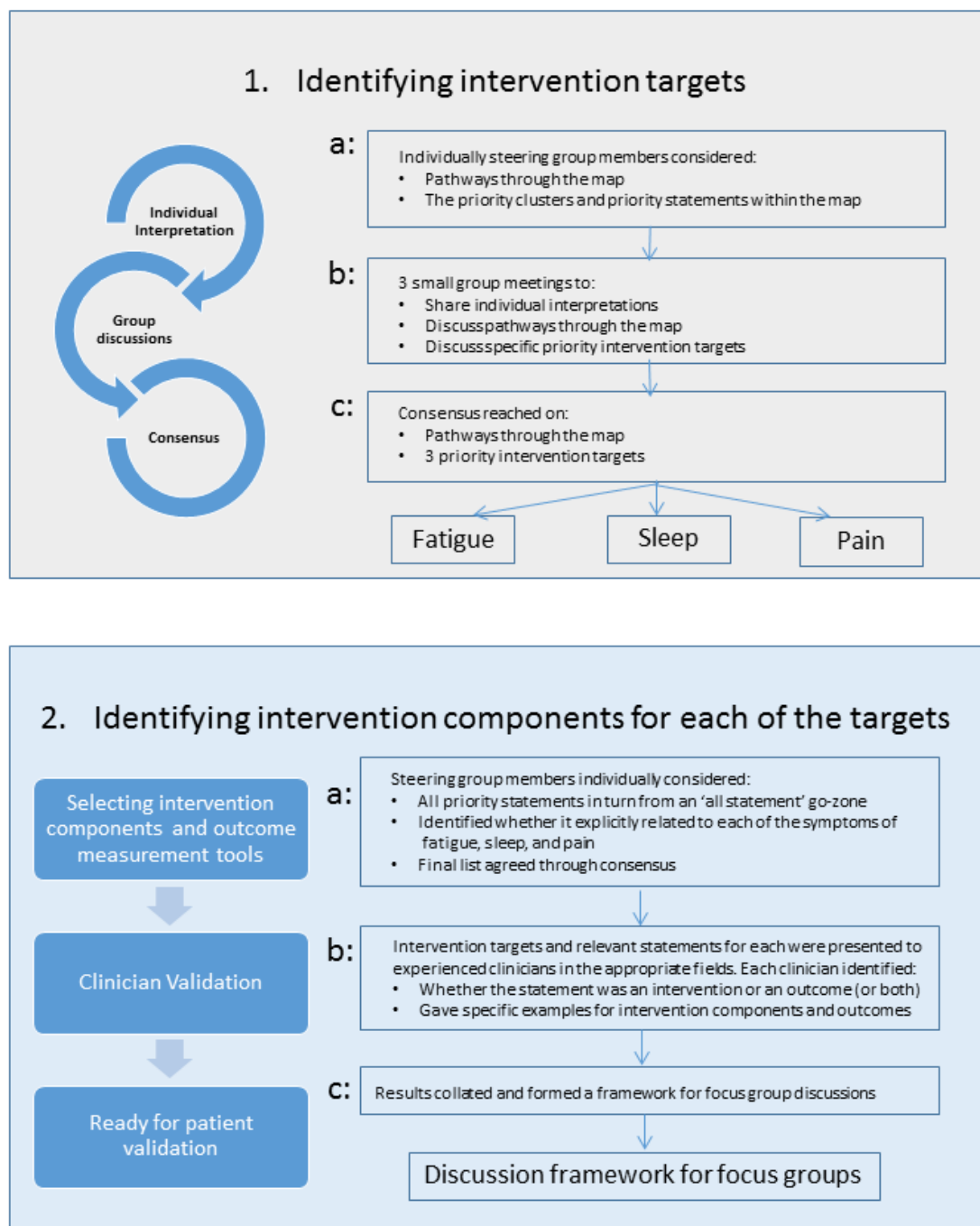


Figure 4:1 Flow chart demonstrating how the concept maps were utilised in the intervention development process

4.3.1 Identifying intervention targets from the concept maps

- a) Firstly, six steering group members (KH, TR, NK, VD, KD, W-FN) individually further examined the concept maps, in order to identify targets for a future intervention plan which will aim to improve participation and ability to perform daily activities for people with PSS. The same steering group members individually considered the clusters in the 7 cluster map (Figure 3:18) initially and drew logical pathways through the map. The pathways were a way of demonstrating how adjacent clusters within the maps may relate to each other. Clusters located near to each other are likely share some similarities with other clusters close by due to being near to each other on the map and it is possible that a cluster will influence its neighbouring clusters in some way.
- b) Secondly, several steering group members (KH, KD, TR, VD) individually considered the maps in light of the cluster importance ratings (Figure 3:19) and the importance of the individual statements within each of the three highest priority clusters (Figure 3:22, Figure 3:23 and Figure 3:24). The steering group members' reported their individual interpretations during three study advisory group meetings. A further member of the steering group who had not been present at the two previous discussions (JN) attended the final group meeting.
- c) During the final steering group discussion meeting, the steering group reached consensus through discussion on the logical pathways through the map and for three specific intervention targets.

4.3.2 Identifying intervention components and outcomes for each of the intervention targets from the priority statements

Next, I created a go zone showing the importance of all individual statements within the concept map. Steering group members considered all statements within the green priority area of the go zone for inclusion as, either an intervention component (as part of a patient focussed intervention), or outcome within the context of each of the three identified intervention targets. Group members individually considered whether each statement explicitly related to each of the identified intervention targets and labelled each with one of four codes (Figure 4:2). Five steering group members took part in this process (KH, TR, VD, KD and JN).

<ul style="list-style-type: none"> • The statement relates explicitly to the intervention target - Include
<ul style="list-style-type: none"> • The statement relates to the overarching theme but is not specific to the intervention target – Exclude
<ul style="list-style-type: none"> • The statement is not patient focussed - Exclude
<ul style="list-style-type: none"> • The statement is not relevant to this intervention target - Exclude

Figure 4:2 Codes used to label each priority go zone statement

We used the following inclusion/exclusion criteria to identify intervention components or outcomes from the priority statements. Statements that steering group members considered as being patient focussed and explicitly relating to the relevant intervention target were included. The statements that group members did not consider patient focussed (e.g. those focussing on political or organisational change) or those that did not explicitly relate to the relevant intervention target were excluded from the intervention component/outcome list. The individual results were discussed and a final list of statements which were labelled as 'include' by any steering group member involved in the coding exercise were listed for consideration by clinicians during the next stage of the process. We generated a final list following a discussion where disagreements over the coding were resolved.

Once the main intervention targets and the priority statements which we considered to be explicitly related to the targets were identified from the concept maps, I presented them to clinicians with experience in at least one of the intervention target areas. The clinicians included physiotherapists (n=3), an occupational therapist (n=1), clinical psychologists (n=2), health psychologists (n=2) and consultant physicians (n=2). I asked the clinicians to consider the intervention targets in their clinical field. For example, clinicians working in the field of chronic pain only considered the priority statements in the context of the intervention target of pain. I asked the clinicians to consider whether each statement could form an intervention, an outcome measure or both. I also asked the clinicians to suggest specific interventions and/or outcome measures for each priority statement. Some clinicians examined the statements individually and fed back their comments. Others discussed their decisions as a group and fed back their ideas as one document. I collated these ideas and have presented them later in the results section of this chapter (see Section 4.4). Following these steps, the intervention target areas were presented to PSS patients and AHMs invited

to qualitative focus group discussions (Chapter 5) and at a patient support group where I was invited to present the results of the study (see Appendix A.7).

The collated results formed the basis of a focus group discussion framework where the potential intervention targets and intervention components were discussed with PSS patients and AHMs (see Chapter 5). I held further discussions with members of the study advisory group to develop the focus group framework questions following the clinician validation exercise.

4.4 Results

4.4.1 Identifying the intervention targets

Please refer to areas 1a, 1b and 1c in the flow chart (Figure 4:1).

4.4.1.1 Interpretation of the map as a whole

There were several ways of interpreting the maps. With this in mind, several members of the steering group first individually considered the cluster map and considered how each cluster related to the others. I presented my initial interpretations to the steering group first and other members shared their interpretations during a discussion. All disagreements were resolved through discussion and resulted in a shared interpretation. We divided the map up by four compass points (see Figure 4:3).

The cluster map includes the Patient empowerment cluster at the centre. The clusters to the North of the map broadly relate to society's response to the disease. To the South: A personal response to the disease; to the West: Environment; to the East: Health (see Figure 4:3).

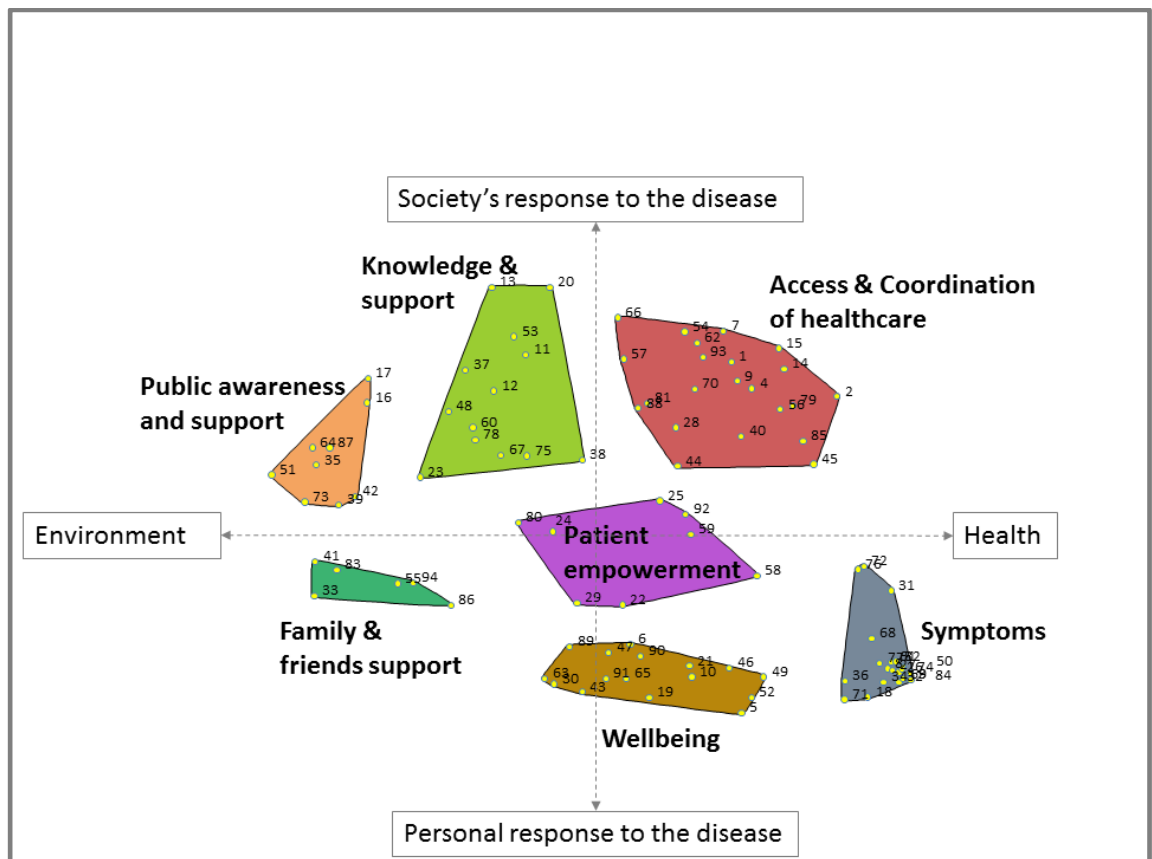


Figure 4:3 The 7 Cluster map with broad theme areas depicted by compass points

We drew several possible pathways through the map. Finally, we reconsidered the cluster rating map (Figure 3:19) and the most important statements within the two most important clusters (Patient empowerment and Symptoms) (Figure 3:22, Figure 3:23). This influenced the direction of the pathways, which we then modified.

4.4.1.2 Potential pathways through the map

Several pathways were drawn through the clusters of the concept map (see Figure 4:4).

Pathway through the Map

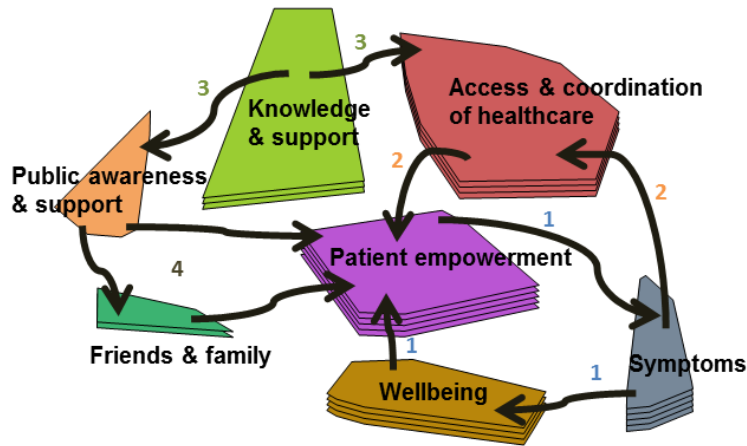


Figure 4:4 Pathways through the concept map

The pathways were split into four sections:

1. In order to empower patients to ‘manage their symptoms themselves’ (#25) and for them to feel that they ‘were being taken seriously’ (#80) by clinicians they should be supported by clinicians to manage their priority symptoms. This in itself could have a positive impact on their wellbeing and result in them feeling more empowered. This section of the pathway is located in the South East corner of the map (see Figure 4:4).
2. The priority symptoms could be addressed through an appropriate and accessible healthcare system. Having an appropriate system in place to help patients manage their symptoms, could be empowering to patients. This section of the pathway is situated in the North East corner of the map (Figure 4:4).
3. Through appropriate knowledge and support such as research ‘to test and develop treatments’ (#20), which would ultimately be delivered through a health care system. Furthermore, as the research and knowledge base

improves, there may be a spill over effect into public awareness of the disease. This section of the pathway is situated in the North West corner of the map (Figure 4:4).

4. Friends and family are more likely to be supportive if they have a better understanding of the disease. Their support could ultimately further empower patients. This section of the pathway is located in the South West corner of the map (Figure 4:4).

4.4.1.3 Identifying intervention targets from the priority clusters and statements

Pathway 1 included the highest priority clusters. We therefore identified this pathway for identifying intervention targets, starting with the most important cluster within the concept map; Patient empowerment.

The most important statements within the Patient empowerment cluster can be viewed in Figure 4:5. Firstly, we put statement #29 'There was a cure', to one side, as there is currently no cure for PSS. Next, we considered statement #80 'Felt they were being taken seriously'. In order to take patients seriously, clinicians should consider what is of importance to their patients. Therefore #25 'Have support to manage their symptoms themselves' is key.

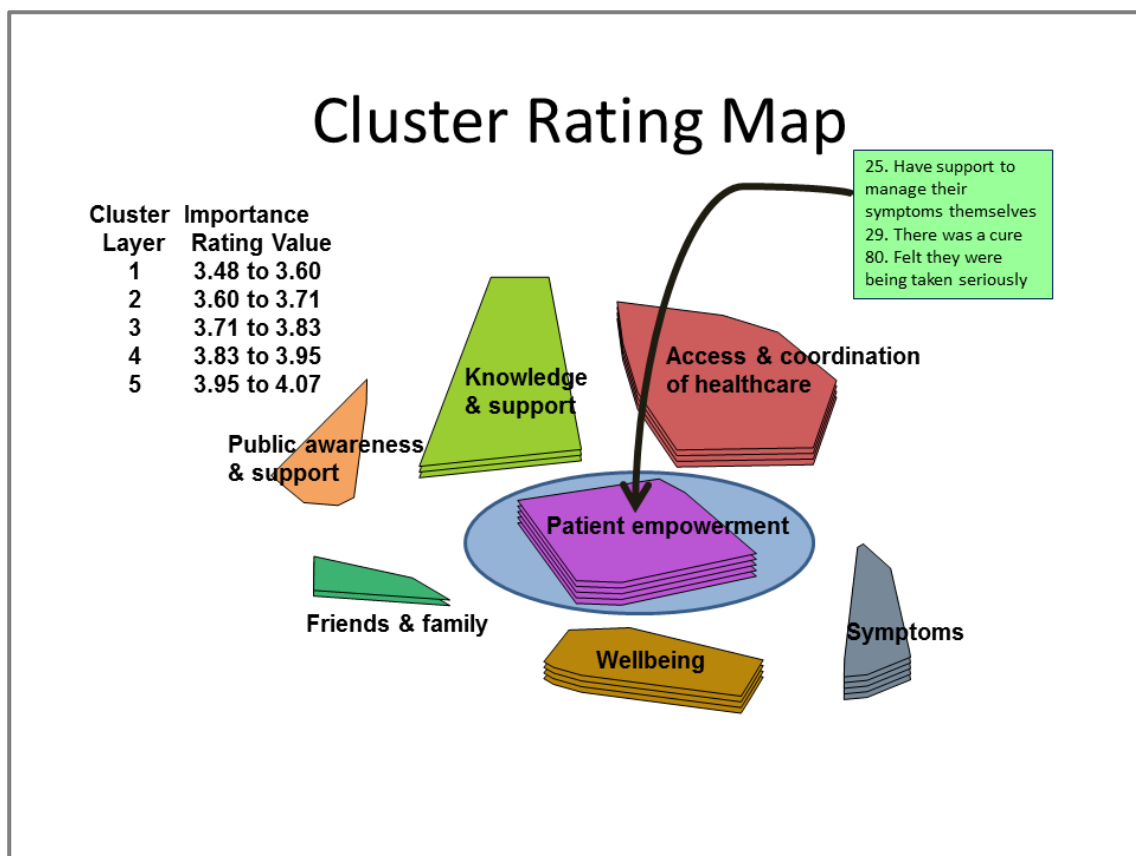


Figure 4:5 Cluster rating map showing the Patient empowerment cluster priority statements

Next, we considered which clusters related to these priority statements. In order to support patients to manage their symptoms themselves, it is necessary to establish which the priority symptoms are. Therefore statement #25 *'Have support to manage their symptoms themselves'* immediately led us to consider the Symptoms cluster. The important symptoms (symptoms which fell within the green go-zone) within the Symptoms cluster were considered (see Figure 4:6). These priority symptoms included symptoms which relate to **fatigue** (#18 *'were less fatigued'* and #76 *'fatigue was better managed/treated'*); **sleep disturbances** (#71 *'were able to sleep better'*), **pain** (#50 *'have less pain'*); **oral dryness** (#34 *'swallowing was easier'*, #68 *'have healthy teeth and/or comfortable dentures'*, #69 *'their throat was less dry'*) and **ocular dryness** (#32 *'their vision was not impaired'*, #61 *'their eyes were more comfortable'* and #84 *'their eyes were less dry'*).

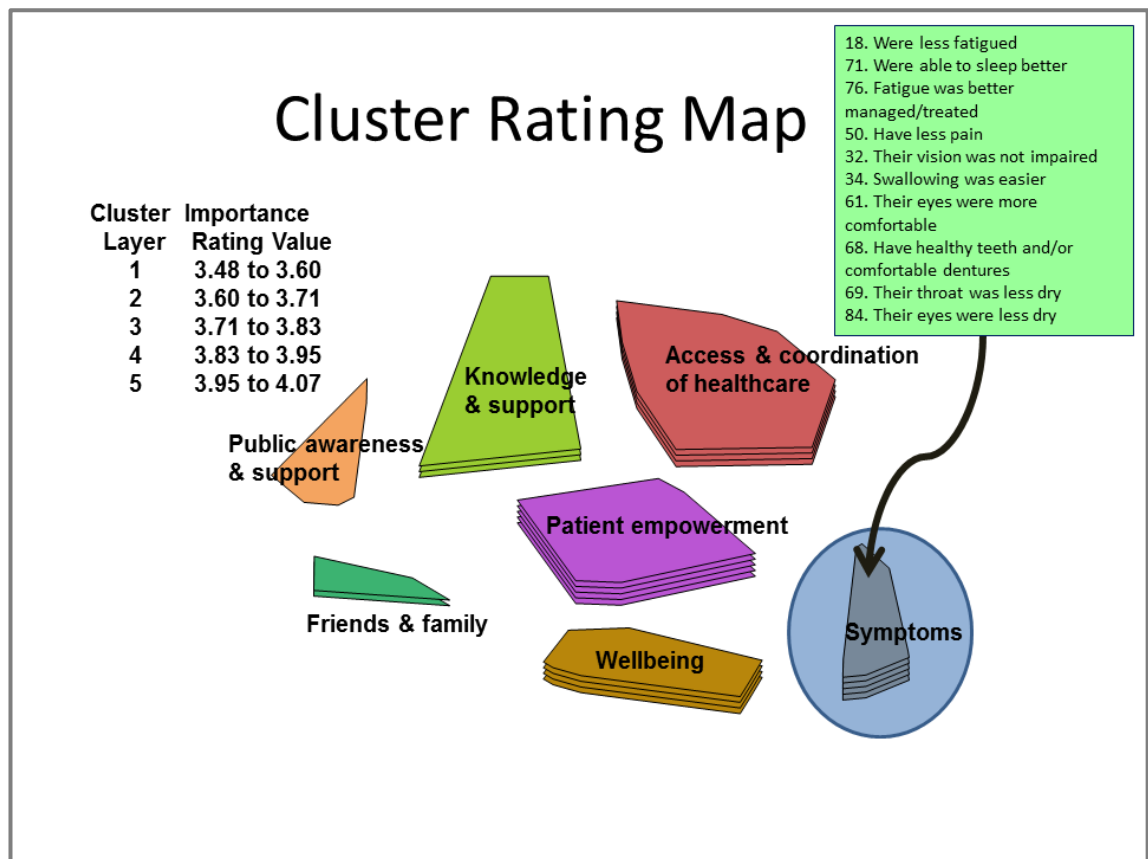


Figure 4:6 Cluster rating map showing Symptoms priority statements

However not all symptoms actually ended up being located within the Symptoms cluster following the concept mapping process. Three statements, which could be considered as being mental health symptoms, ended up being located in the Wellbeing cluster. These included the #10 '*Were less stressed or worried*', #49 '*Could improve their concentration*' and #52 '*Their mood was better*'. All three of these statements were located within the concept map relatively close to the Symptoms cluster, but were not incorporated within this cluster during the cluster analysis. This is because the participants regarded these statements belonging conceptually to a Wellbeing theme. However, none of these statements (#10, #49 or #52) featured in the green go zone area of the Wellbeing cluster and therefore were not regarded as being priorities by PSS patients and AHMs. The priority statements within the Wellbeing cluster can be viewed in Figure 4:7. The steering group considered several of the statements within this third highest priority cluster, as being components of an intervention rather than a target. For example #65 '*Learn to balance their activity and rest*' might be considered as a component of a fatigue intervention in other conditions e.g. chronic fatigue syndrome (White *et al.*, 2011).

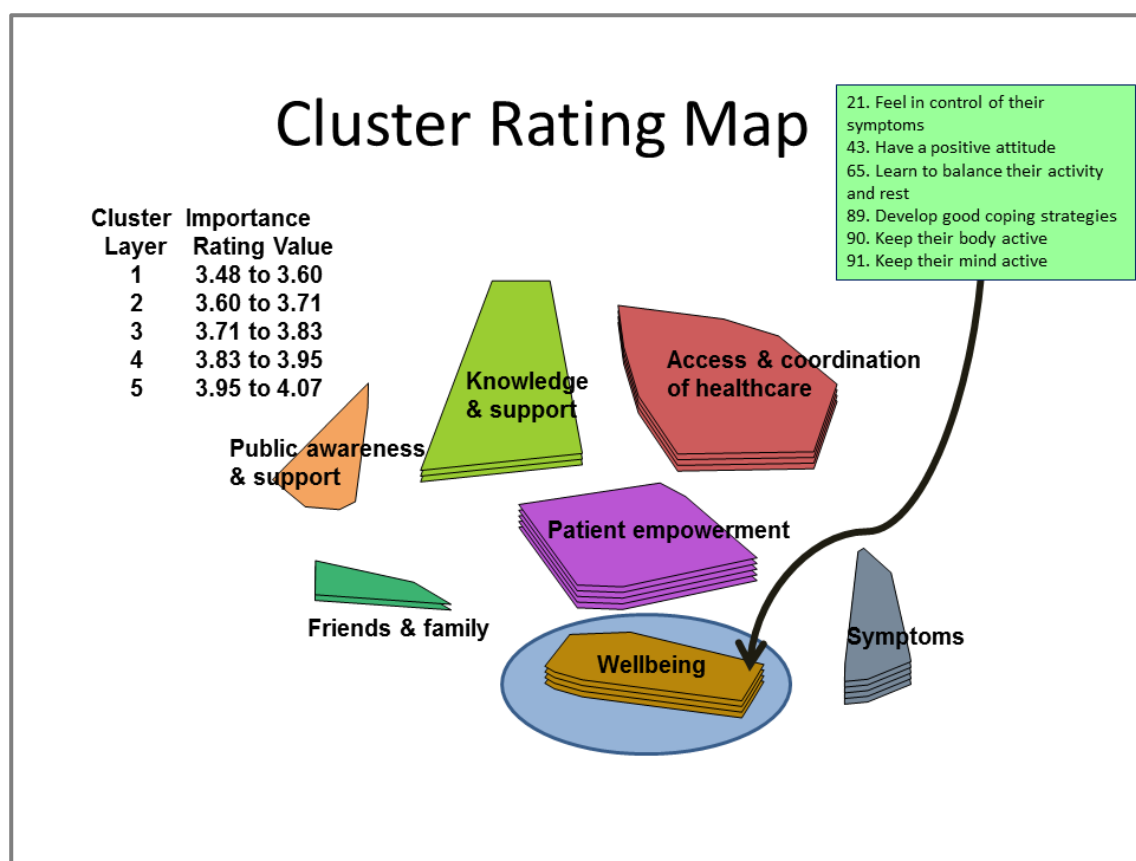


Figure 4:7 Cluster rating map showing Wellbeing priority statements

4.4.1.4 Consensus on intervention targets

During the third steering group meeting, members agreed that Section 1 of the pathway within the concept map (see Figure 4:4) was a priority area to focus intervention development goals as this area of the map contained the top priority clusters. Therefore, the intervention development focus should be on targeting priority symptoms in order to improve patients' wellbeing and further empower them.

Although five main symptom target areas were identified (sleep, fatigue, pain, oral dryness and ocular dryness), the group agreed that dryness symptoms are routinely addressed in clinics. There are systemic and topical treatments for both oral and ocular dryness and patients in the UK can be referred to an oral health physician or dentist and to an ophthalmologist for specialist care (Price, 2016a). Non-pharmacological treatments for sleep, pain and fatigue are not regularly addressed with PSS patients in the UK (Lord *et al.*, 2009; Ng and Bowman, 2010; Hart *et al.*, 2016) and therefore these

needs remain unmet for many patients. The steering group therefore considered these three symptoms as being priority targets for an intervention plan (see Figure 4:8).

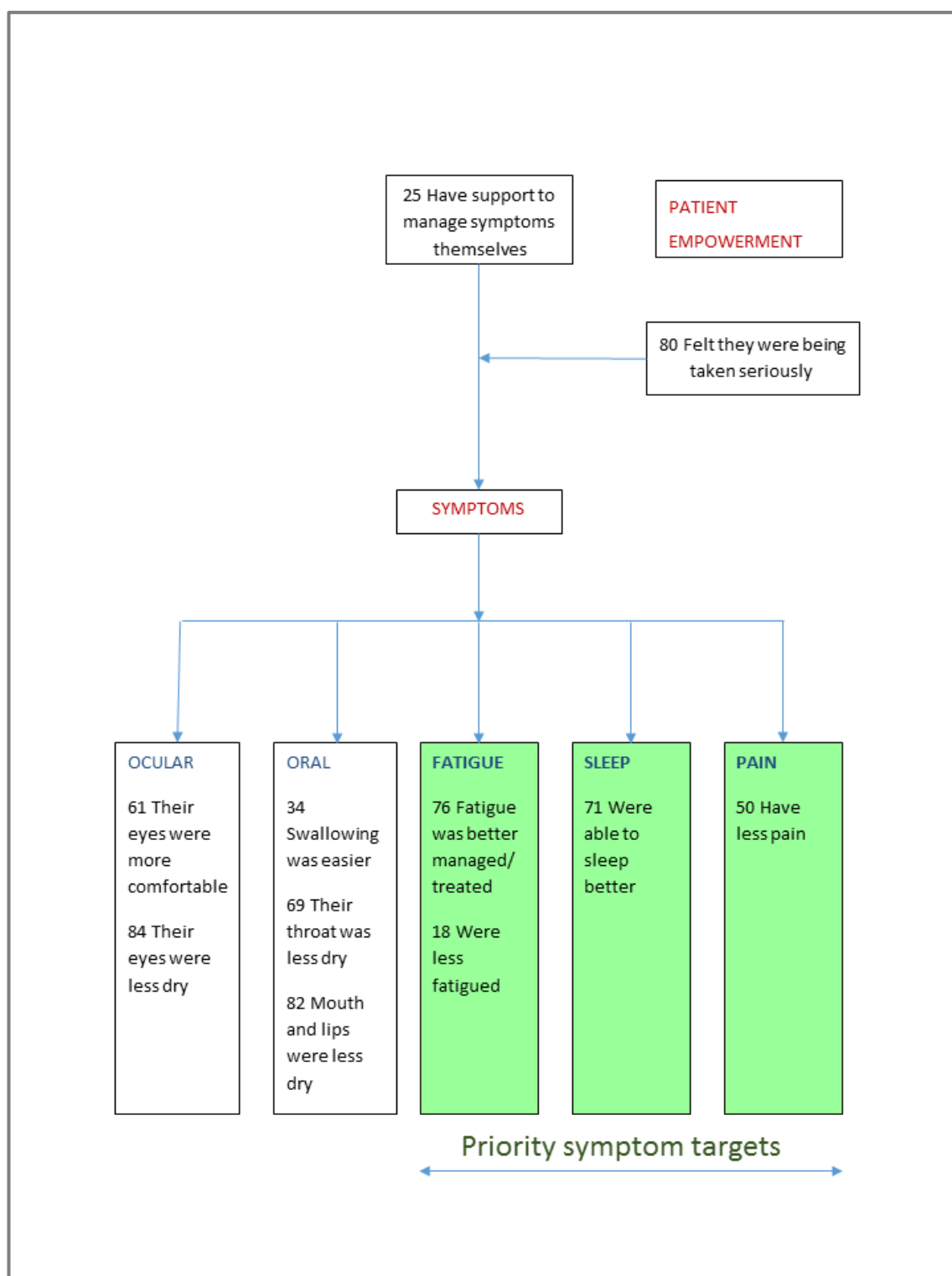


Figure 4:8 Priority symptom targets and the priority statements referring to them

4.4.2 Identifying the intervention components for each symptom target

Please refer to areas 2a, 2b and 2c in the flow chart (Figure 4:1).

4.4.2.1 Selecting possible intervention components and outcome measurement tools

The go zone highlights all the priority statements within the concept map. The statements within the green priority 'go zone' area can be viewed in Figure 4:9 below.

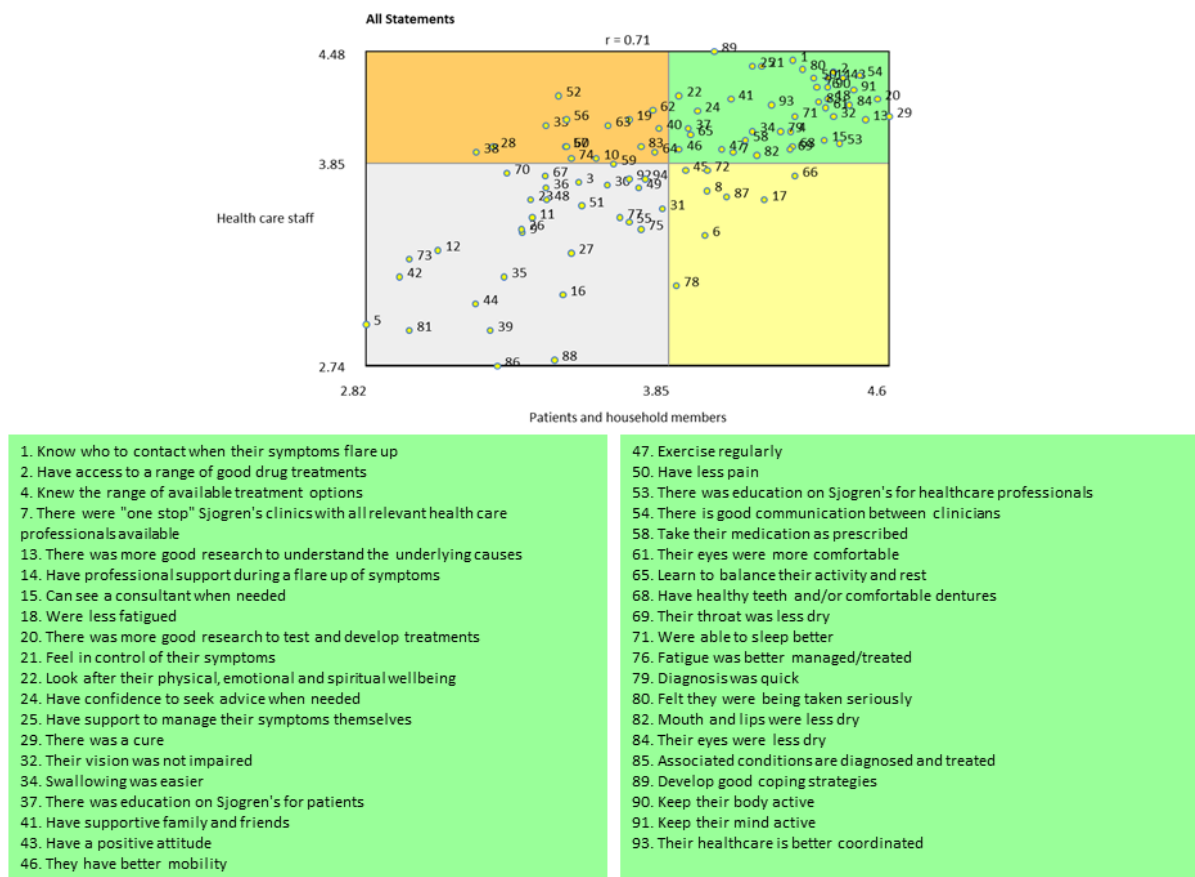


Figure 4:9 Go zone of all statements with the most important statements highlighted in the green area

4.4.2.2 Steering group interpretation session to reach consensus on intervention targets

Following individual consideration of each priority statement within the context of each priority symptom target, the steering group identified a list of priority statements, which they considered as relating explicitly to fatigue, sleep and pain.

These statements are identified in Table 4-1 (statements relating to a fatigue

intervention target), Table 4-2 (statements relating to a sleep intervention target) and Table 4-3 (statements relating to a pain intervention target) below.

Potential components/facilitators or outcomes for a fatigue intervention identified from the priority concept statements within the concept map
<p>4. Knew the range of available treatment options</p> <p>6. They have a good diet</p> <p>10. Were less stressed or worried</p> <p>18. Were less fatigued</p> <p>19. Could come to terms with their symptoms</p> <p>25. Have support to manage their symptoms themselves</p> <p>38. Could access support to help set personal goals</p> <p>46. They have better mobility</p> <p>47. Exercise regularly</p> <p>50. Have less pain</p> <p>52. Their mood was better</p> <p>63. Could come to term with their limitations</p> <p>64. Employers were aware of things they could do in the workplace for people with Sjögren's</p> <p>65. Learn to balance their activity and rest</p> <p>71. Were able to sleep better</p> <p>89. Develop good coping strategies</p>

Table 4-1 Priority statements identified by the steering group as explicitly relating to the fatigue intervention target

Potential components/facilitators or outcomes for a sleep intervention identified from the priority concept statements within the concept map
<p>4. Knew the range of available treatment options</p> <p>6. They have a good diet</p> <p>10. Were less stressed or worried</p> <p>18. Were less fatigued</p> <p>21. Feel in control of their symptoms</p> <p>25. Have support to manage their symptoms themselves</p> <p>38. Could access support to help set personal goals</p> <p>47. Exercise regularly</p> <p>50. Have less pain</p> <p>65. Learn to balance their activity and rest</p> <p>71. Were able to sleep better</p> <p>82. Mouth and lips were less dry</p> <p>89. Develop good coping strategies</p> <p>90. Keep their body active</p>

Table 4-2 Priority statements identified by the steering group as explicitly relating to the sleep intervention target

Potential components/facilitators or outcomes for a pain intervention identified from the priority concept statements within the concept map
<p>4. Knew the range of available treatment options</p> <p>10. Were less stressed or worried</p> <p>18. Were less fatigued</p> <p>19. Could come to term with their symptoms</p> <p>21. Feel in control of their symptoms</p> <p>25. Have support to manage their symptoms themselves</p> <p>46. They have better mobility</p> <p>50. Have less pain</p> <p>52. Their mood was better</p> <p>58. Take their medication as prescribed</p> <p>65. Learn to balance their activity and rest</p> <p>89. Develop good coping strategies</p>

Table 4-3 Priority statements identified by the steering group as explicitly relating to the pain intervention target

4.4.2.3 Clinician validation

Following the consultation with clinicians working in each of the relevant fields of chronic fatigue, sleep disturbances and chronic pain, the clinicians identified specific priority statements as being intervention targets and/or outcomes. The clinicians gave specific examples of interventions and outcomes. These can be seen in Table 4-4 (for a fatigue intervention target), Table 4-5 (for a sleep intervention target) and Table 4-6 (for a pain intervention target).

The clinicians regarded some statements as being a potential intervention component/facilitator for a particular symptom target and they regarded others as being an outcome. They considered some statements as being both an intervention component and an outcome and provided examples, which can be seen in the tables.

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
4. Knew the range of available treatment options	Access & Coordination of Healthcare	Yes	At first appointment give information and make treatment plan in collaboration with patient	No	N/A
6. They have a good diet	Wellbeing	Yes	Advice on caffeine, sugar and fluid intake, general healthy eating, swallowing with a dry mouth	Yes	Food diaries for caffeine and sugar intake (when used to fight fatigue)
10. Were less stressed or worried	Wellbeing	Yes	CBT	Yes	Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1986)
18. Were less fatigued	Symptoms	No	N/A	Yes	Fatigue VAS, ESSPRI (Seror <i>et al.</i> , 2011)
19. Could come to terms with their symptoms	Wellbeing	Yes	ACT	Yes	Acceptance and Action Scale II (Bond <i>et al.</i> , 2011)
25. Have support to manage their symptoms themselves	Patient Empowerment	Yes	Activity management, pacing, GET, CBT		Fatigue VAS, ESSPRI

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
38. Could access support to help set personal goals	Knowledge & Support	Yes	Goal setting	Yes	Canadian Occupational Performance Measure (Law <i>et al.</i> , 2005a)
46. They have better mobility	Wellbeing	Yes	GET/exercises to activate specific targeted muscle groups	Yes	Increase in step count, Increase in timed physical activity, increase in mobility, SF36 physical function score
47. Exercise regularly	Wellbeing	Yes	Goal setting and GET	Yes	Increase in step count, Increase in timed physical activity
50. Have less pain	Symptoms	Yes	Pacing/balancing activity/GET/ CBT/ ACT/ Mindfulness	Yes	Pain VAS, ESSPRI
52. Their mood was better	Wellbeing	Yes	CBT, behavioural activation	Yes	HADs
63. Could come to terms with their limitations	Wellbeing	Yes	ACT	Yes	Acceptance and Action Scale II
64. Employers were aware of things they could do in the workplace for people with Sjögren's	Public Awareness	Yes	Personalised letter to give to employer with suggested reasonable adjustments, generic leaflet for employer	No	N/A

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
65. Learn to balance their activity and rest	Wellbeing	Yes	Pacing/balancing activity/GET/CBT	Yes	Activity diaries and activity monitor, activity balancing scale (Dur <i>et al.</i> , 2014), Work and Social Adjustment Scale (Mundt <i>et al.</i> , 2002)
71. Were able to sleep better	Symptoms	Yes	CBT-Insomnia	Yes	Sleep diaries/activity monitor
89. Develop good coping strategies	Wellbeing	Yes	Goal setting, CBT, Mindfulness, Pacing	Yes	Brief COPE (Carver, 1997)

ACT = Acceptance and Commitment Therapy, CBT = Cognitive Behavioural Therapy, CBT-Insomnia = Cognitive Behavioural Therapy for Insomnia, ESSPRI = EULAR Sjögren's Syndrome Patient Reported Index GET = Graded Exercise Therapy, HADs = Hospital Anxiety and Depression Scale, VAS = Visual Analogue Scale.

Table 4-4 Intervention components and outcomes identified for a fatigue intervention target by clinicians

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
4. Knew the range of available treatment options	Access & Coordination of Healthcare	Yes	At first appointment give information and make treatment plan in collaboration with patient	No	N/A
6. They have a good diet	Wellbeing	Yes	Advice on caffeine intake	Yes	Diary recording of caffeine intake
10. Were less stressed or worried	Wellbeing	Yes	Address worrying thoughts, notebook by the bed (component of CBT –Insomnia intervention)	Yes	HADs
18. Were less fatigued	Symptoms	No	N/A	Yes	Fatigue VAS, ESSPRI
21. Feel in control of their symptoms	Wellbeing	Yes	Behavioural changes as part of CBT-Insomnia intervention	Yes	Sleep diaries
25. Have support to manage their symptoms themselves	Patient Empowerment	Yes	CBT-Insomnia		Sleep diaries
38. Could access support to help set personal goals	Knowledge & Support	Yes	CBT-Insomnia	Yes	Sleep diary/ actigraphy
47. Exercise regularly	Wellbeing	Yes	Goal setting, GET, CBT	No	N/A

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
50. Have less pain	Symptoms	Yes	Mindfulness, pain management techniques, relaxation, warm baths before bed, ACT	Yes	Pain VAS, ESSPRI
71. Were able to sleep better	Symptoms	Yes	CBT-Insomnia	Yes	Sleep diaries/ actigraphy
82. Mouth and lips were less dry	Symptoms	Yes	Glass of water by the bed/use of artificial saliva	No	N/A
89. Develop good coping strategies	Wellbeing	Yes	CBT-Insomnia	Yes	Brief COPE
90. Keep their body active	Wellbeing	Yes	GET, general exercise	No	

Table 4-5 Intervention components and outcomes identified for a sleep intervention target by clinicians

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
4. Knew the range of available treatment options	Access & Coordination of Healthcare	Yes	At first appointment give information and make treatment plan in collaboration with patient	No	N/A
10. Were less stressed or worried	Wellbeing	Yes	CBT, mindfulness-based stress reduction	Yes	HADs
18. Were less fatigued	Symptoms	Yes	Activity management, pacing	Yes	Fatigue VAS, ESSPRI
19. Could come to terms with their symptoms	Wellbeing	Yes	ACT	Yes	Acceptance and Action Scale II (Bond <i>et al.</i> , 2011)
21. Feel in control of their symptoms	Wellbeing	Yes	CBT, GET, ACT	Yes	Revised Illness Perception Questionnaire (Moss-Morris <i>et al.</i> , 2002)
25. Have support to manage their symptoms themselves	Patient Empowerment	Yes	CBT, GET, ACT	Yes	Revised Illness Perception Questionnaire (Moss-Morris <i>et al.</i> , 2002)
46. They have better mobility	Wellbeing	Yes	GET/Physiotherapy targeted exercises	No	N/A
50. Have less pain	Symptoms	Yes	CBT, ACT	Yes	Pain VAS, ESSPRI

Go zone statements	Cluster	Intervention?	Examples	Outcome?	Examples
52. Their mood was better	Wellbeing	Yes	CBT, behavioural activation	Yes	HADs
58. Take their medication as prescribed		Yes	If relevant, pain medication adherence therapy	Yes	Medication adherence scales (Nguyen <i>et al.</i> , 2014)
65. Learn to balance their activity and rest	Wellbeing	Yes	Pacing/balancing activity/GET/CBT	Yes	Activity diaries and activity monitor, activity balancing scale (Dur <i>et al.</i> , 2014)
89. Develop good coping strategies	Wellbeing	Yes	CBT, ACT	Yes	Brief COPE

Table 4-6 Intervention components and outcomes identified for a pain intervention target by clinicians

4.4.2.4 Focus group discussion framework

After collating the feedback from the clinicians, I consulted with the study advisory group and drew up a framework of focus group questions to guide focus group discussions on the intervention target symptoms of fatigue, sleep and pain. It was important to ask people with the lived experience of PSS about their experiences of each of these symptoms prior to discussing potential intervention components. Therefore, focus group discussions on each of the areas started with asking people with the lived experiences of PSS about their individual experiences of the symptoms. The second part of the focus group discussion framework revolved around asking people about what kind of help they have sought for these symptoms (if any). The final part of the focus group discussion framework was for the facilitator to present some of the intervention components brought up during the clinician validation. The purpose was to ascertain whether these types of intervention components are likely to be acceptable and therefore be received well by people with PSS and their families. The outline of the discussion framework can be viewed in Table 4-7.

Outline focus group discussion framework for each symptom target
A i) Do people with PSS have difficulty with this symptom? ii) What specific fatigue difficulties do you/your relative experience? iii) Have the difficulties changed over time? How? iv) Does this symptom impact on everyday life? How? v) How do you/your relative currently manage this symptom?
B i) Have you/your relative sought help for fatigue? From where or whom? ii) Do you talk to others about it? Who? How do they respond? iii) What kind of support/treatment have you had? Did this help? In what way?
C i) Here are some possible non-drug intervention solutions. What do you think about each? (Intervention components identified in Table 4-4, Table 4-5 and Table 4-6)
D) How would you like an intervention to be provided? e.g. in groups, one to one, printed information etc.

Table 4-7 Future focus group discussion framework for each symptom target

4.5 Discussion

By carefully going through a process of examining the concept maps in detail with steering group members and careful interpretation of the results together, I have been able to identify priority intervention targets for PSS patients. Fatigue, sleep disturbances, pain, oral and ocular dryness have all been identified as symptoms which impact on patients with PSS ability to participate fully in daily life and carry out their daily activities. Dryness is a feature which is well recognised and there are established treatments which are recommended (Foulks *et al.*, 2015; Vivino *et al.*, 2015; Brito-Zeron *et al.*, 2016). However, fatigue, sleep and pain are needs which are infrequently addressed in the clinical setting and therefore they remain unmet (Segal *et al.*, 2009; Ng *et al.*, 2011; Hackett *et al.*, 2016a). Consequently, we considered these three symptoms as being ideal intervention targets.

Through discussing these intervention targets in more detail and considering further priority statements from all clusters within the concept maps, in collaboration with the steering group members, I have been able to identify some interventions (or facilitators) and outcomes from within the concept maps. The intervention components identified through the clinician validation process are more likely to be acceptable and feasible for delivery by clinicians within a clinical setting due to involving these key stakeholders in the process (Gitlin, 2013). The clinician validation process has fleshed out the priorities and given some realistic suggestions as to how each of these intervention targets might be addressed. The next step is to discuss these further with PSS patients and their family members to establish firstly whether they believe these intervention components and symptom targets should be addressed within PSS care. Secondly, if these intervention components are regarded by people with the lived experience of the condition as being both acceptable and important, it is important to establish how these components should be delivered.

This next stage has addressed the high priority pathway within the concept map. There are alternative pathways, which are considered as being less of a priority. The lower priorities could also be addressed in a future intervention development plan.

Alternative clusters (such as Access and coordination of healthcare) and pathways

within the map, could also be addressed to provide better holistic care and social support to improve the quality of life in PSS patients.

4.6 Summary

The work presented in this chapter has provided a focus group discussion framework to further explore the high priority intervention pathway. The following two chapters (Chapters 5 & 6) describe a focus group study and the emergent themes, which resulted from using this discussion framework with PSS patients and their family members.

Chapter 5. A qualitative focus group study to explore the experiences and impact of fatigue, sleep disturbances and pain/discomfort

The previous chapter explained how the concept maps were utilised to identify specific unmet needs which could be targeted in future interventions to improve participation and the ability to perform daily activities. In this chapter, I describe the methods used to carry out several focus groups, in which I further discussed these unmet needs with patients and their spouses. I describe how I analysed the focus group data and present the results of how people with the lived experience of PSS, describe their fatigue, sleep disturbances and pain. I also discuss the impact of these symptoms on activities of daily living and participation.

5.1 Method

5.1.1 Aims

The aim of this study was to discover more about the PSS symptoms of fatigue, sleep disturbances and pain from those with the lived experience of PSS.

5.1.2 Study design

I chose qualitative focus groups in order to meet the aims of this study. Focus groups use group interaction to collect data, as participants are encouraged to talk with each other, thus enabling them to comment on each other's experiences and viewpoints, whilst being able to ask each other questions and provide anecdotes (Kitzinger, 1995). Group discussion is appropriate when the researcher has a series of open-ended questions, as participants are able to explore these with each other and focus on the issues they perceive as being important, using their own vocabulary (Kitzinger, 1995). Furthermore, focus groups can be used in the development phase of complex intervention development, particularly if a systematic review of the existing literature has not answered questions about the effectiveness of existing interventions (Craig *et al.*, 2006).

5.1.3 Ethical approvals

In order to conduct this study, I applied for a substantial amendment to the original concept mapping study approvals (13/NI/0190, IRAS Ref: 125562). I drew up new participant information sheets and consent forms for this section of the study which were submitted during the application process. This documentation including the letter from the ethical board granting this substantial amendment can be viewed in the Appendices (Section A.2).

5.1.4 Recruitment and sampling strategy

I posted invitation packs to 62 potential participants. The potential participants were 44 PSS patients and 18 AHMs who had previously been recruited from the Newcastle upon Tyne site and had taken part in the earlier concept mapping study and had given consent to be invited to take part in future research studies. I did not send out reminder invitations. The pack included the participant information sheet, a reply form and a consent form (See Appendices, Section A.2.2 and A.2.3). As ethical and NHS Trust approvals were in place for the Newcastle site, participants were recruited from this site. The largest number of participants had also been recruited from this single site during the previous concept mapping study, as it is the host site of the UKPSSR and a regional specialist centre. This sampling strategy can be classified as criterion sampling (Patton, 2002) with location being the core sampling criteria. However, in practice, it is more representative of convenience sampling. Convenience sampling, albeit commonly used in qualitative research is not an ideal approach (Patton, 2002). However, I should note that this was not a stand-alone qualitative study, but an exploratory phase, following on from the prior work. Also a previous PSS study which recruited patients from the Newcastle site demonstrated that the Newcastle patients who took part were reasonably representative of the whole UKPSSR cohort (Hackett *et al.*, 2012a).

I asked potential participants to reply using an enclosed reply form and to indicate whether they wished to participate in any of the focus groups. I also asked potential participants to suggest days of the week and times during the day when they would likely be available for a focus group. I subsequently planned the timing of the groups around the availability of both the facilitators and participants. Participants provided informed consent and signed consent forms prior to attending the focus groups.

5.1.5 Structure of the focus groups

The focus group meetings took place during a weekday morning in a meeting room in the Newcastle upon Tyne Hospitals NHS Foundation Trust. I allocated two hours for each focus group. This allowed time for participants to settle and help themselves to a drink. At the beginning of each meeting, I briefly explained the results of the previous concept mapping study to participants then introduced the questions which guided the topic discussions (see Table 5-1).

The conversations were structured around exploring:

- Their experiences of the symptoms of fatigue, sleep disturbances and pain,
- The strategies patients use to manage them
- The impact these symptoms have on participation.

The focus of this chapter is on experiences of symptoms. I present the results of the other two elements, together with participants' thoughts on potential intervention strategies suggested by clinicians and potential modes of delivering future non-pharmacological interventions in the following chapter (Chapter 6 and 7).

Topic guide
Do you (or your relative) experience any difficulties with fatigue? What are they? Do you (or your relative) experience any difficulties with sleep? What are they? Do you (or your relative) experience any difficulties with pain? What are they?

Table 5-1 Topic guide used to explore symptoms of fatigue, sleep disturbances and pain

At the beginning of each focus group, I gave participants handouts with the outline structure of each session and a pen. I explained to them that they could write anything down on the paper and these would be collected in at the end. I divided each focus group session into two phases with a 15-20 minute break in the middle. Each phase lasted between 30 and 50 minutes. The meetings were audio recorded and these audio recordings were transcribed verbatim. Participants were reimbursed for their travel and drinks and snacks were available throughout the sessions. Participants could

attend more than one focus group meeting if they wished, as the discussion topics were different at each meeting.

I facilitated the three focus group sessions, which I structured around the following topics: sleep disturbances; fatigue; pain and potential modes of delivering future interventions. Dr Vincent Deary co-facilitated the meetings with me and took field notes. Dr Deary and I both work as clinicians in the Newcastle CRESTA Fatigue clinic (Hackett *et al.*, 2016b), and we both have extensive experience of working clinically as therapists with patients with chronic fatigue, chronic pain and long-term conditions. Dr Deary had not met any of the participants prior to the focus groups. I had previously met several participants during the course of my clinical work and had met two participants during the earlier concept mapping study, at the face-to-face group brainstorming session. At the end of each focus group, I summarised the topics of the conversation as an informal way of checking my interpretation of the conversations with the group members: this represents a modest version of ‘member checking’ (Lincoln and Guba, 1985).

5.1.6 Data analysis

I used thematic analysis to analyse the data (Braun and Clarke, 2006; Braun and Clarke, 2013; Braun and Clarke, 2014) as it allows for the identification and analysis of patterns within the data. I use thematic analysis as an essentialist, or realist method in order to report the experiences, meanings and the reality of participants (Braun and Clarke, 2014).

I use thematic analysis to reflect the reality of the participants’ viewpoints and experiences in the following chapters (Chapters 6 and 7), I attempt to apply the participants’ reality to the wider context of how services might be delivered for PSS patients in the future, within an NHS setting. I have addressed my analysis from a critical realist standpoint (Pawson and Tilley, 1997; Willig, 1999). This approach acknowledges that our experiences, perspectives and theories shape our understanding of the world (Maxwell, 2012), therefore there is no possibility of accurately obtaining a ‘*God’s eye view*’ (Putnam, 1989).

I conducted the thematic analysis in six phases, as described by Braun and Clarke (2006):

1. I familiarised myself with the data by listening through the audio recordings and reading through the transcripts. Whilst doing this I noted down my initial ideas.
2. Next, I generated initial codes from the data. I recorded the codes in an Excel spreadsheet and pasted in sections of transcript, which related to those codes in adjacent cells.
3. I then examined the codes and grouped those together which conveyed similar meanings. This resulted in the generation of higher order themes.
4. I reviewed these themes in relation to the coded extracts of text from the transcripts to ensure that they worked within the context of the whole dataset. These themes and the codes within them, were then reviewed by a second researcher (Dr Tim Rapley) and regularly discussed with him. They were also reviewed by other members of the supervisory team to improve analytical rigour (Fernald and Duclos, 2005).
5. I continued to analyse and refine the specifics of the themes and the overall story, which the analysis presents.
6. I wrote up the analysis, which went through several iterations. I selected appropriate sections of text to describe the themes, which I had interpreted from the data.

5.2 Results

I received postal responses from 27 out of the 62 PSS patients and AHMs who I had invited to take part (44% response rate). Nineteen respondents indicated that they would like to take part in a focus group. Thirteen were able to attend one or more focus groups, including 10 patients with PSS (8 female and 2 male) and 3 AHMs (2 female and 1 male). Table 5-2 shows the demographic details of the focus group participants and indicates which meetings they attended as well as the fatigue, pain and dryness symptom scores for the PSS participants. These scores were recorded during the previous concept mapping study. The focus groups all took place late morning during the week. A second table provides demographic data for those who provided consent to take part in the focus groups, but were unable to attend (see Table 5-3).

I observed few differences between those who were able to attend a focus group meeting and those who were not. Of note, one PSS patient who provided consent but was unable to attend was in full-time employment. The patients in the non-attendance group also seemed to have higher dryness scores than those who were able to attend.

Participants		Gender	Age	Employ- ment status	Attend FG1	Attend FG2	Attend FG3	Years since diagnosis	Pain (0-100) [†]	Bodily Pain*	Fatigue (0-100) [†]	Vitality*	Dryness (0-100) [†]
PP1	Patient	M	62	Unemployed	Yes	Yes	No	4	49	34.2	53	31.8	69
PP2	Patient	F	73	Retired	Yes	No	No	26	34	46.7	72	46.7	58
PP3	Patient	F	46	Unemployed	Yes	Yes	Yes	10	16	51.51	96	28.8	49
PP4	Patient	F	74	Retired	Yes	No	No	11	23	42.6	82	22.9	69
PP5	Patient	M	59	Emp P/T	Yes	Yes	Yes	4	12	55.5	39	46.7	11
PP6	Patient	F	54	Unemployed	Yes	Yes	Yes	2	82	26.5	90	22.9	37
PP7	Patient	F	65	Emp P/T	Yes	Yes	Yes	7	16	46.3	28	52.6	33
PP8	Patient	F	77	Retired	No	Yes	Yes	12	23	42.6	93	22.9	66
PP9	Patient	F	75	Retired	No	Yes	Yes	31	23	46.7	29	52.6	45
PP10	Patient	F	68	Retired	No	No	Yes	4	30	42.2	74	40.7	59
AHM1	Spouse	F	66	Retired	Yes	Yes	No	4					
AHM2	Spouse	M	60	Retired	No	Yes	Yes	12					
AHM3	Spouse	M	77	Retired	No	Yes	Yes	31					
Mean (SD)			66 (10)		Total 8	Total 10	Total 9	12 (10)	28 (21)	45 (8)	66 (26)	36.8 (12)	50 (19)

[†] VAS *SF-36 domain norm-based scores (US norms = 50 (SD 10)), FG = Focus Group, Emp P/T = Employed part-time

Table 5-2 Focus group participants' attendance and demographics

Participants		Gender	Age	Employ- ment status	Years since diagnosis	Pain (0-100) [†]	Bodily Pain*	Fatigue (0-100) [†]	Vitality*	Dryness (0-100) [†]
PP11	Patient	F	60	Retired	4	81	34.6	100	22.9	99
PP12	Patient	F	52	Emp F/T	26	7	55.6	26	46.7	84
PP13	Patient	F	70	Retired	31	29	47.5	71	40.1	79
PP14	Patient	F	56	Emp P/T	8	63	30.6	53	31.8	88
PP15	Patient	F	77	Retired	9	21	46.7	22	46.7	52
AHM4	Spouse	M	67	Retired	8					
Mean (SD)			64 (9)		14 (11)	40 (31)	43 (10)	54 (33)	38 (10)	80 (18)

[†]VAS *SF-36 domain norm-based scores (US norms = 50 (SD 10)), FG = Focus Group, Emp F/T = Employed full-time, Emp P/T = Employed part-time

Table 5-3 Demographic details who provided consent, but were unable to attend a focus group

In the following text, each participant is referred to by their code number in Table 5-2; focus group facilitators are referred to by our first names and the groups are coded according to the session number; e.g. FG1A is the first half of focus group 1 and FG3B is the second half of the third focus group.

5.2.1 Living with symptoms of PSS

5.2.1.1 Symptoms as a whole

The previous concept mapping study (see Chapter 3) demonstrated that symptoms of sleep disturbances, fatigue and pain were all deemed to interfere with participation in daily activities, in addition to oral and ocular dryness. Focus group participants concurred with these findings.

In explaining what the terms sleep disturbances, fatigue and pain meant to them, participants worked to question and deconstruct this terminology whilst attempting to explain specifically the impact these symptoms had on their daily lives.

Prior to giving a detailed description about each individual symptom, patients explained what it was like living with a range of PSS symptoms. They explained that this was challenging for a variety of reasons. Firstly, these symptoms can seem as though they are invisible to others. One patient described how even during a flare of symptoms, her friends would say to her:

PP8 *“Well, you look alright [Yeah]. You know, you look fine,” they’ll say, don’t they? (FG2B 607-609)*

If others could not visualise the flare of symptoms, as they would if it were *‘a broken leg’* (AHM2 FG2A 265), this would mean that people they meet on a daily basis *‘don’t know that you’re not well’* (PP7 FG3A 710).

Due to the invisible nature of the symptoms, patients often struggled to meet the expectations of others. This was in part because other *‘people think that you should be able to keep doing everything you used to do’* (PP5 FG1B 1469-70). Others sometimes struggled to understand that the impact of the symptoms means that their colleague, friend or

relative with PSS, may no longer have capacity to do some of the things they used to do with relative ease.

Another important feature of PSS symptoms was that they rarely occur in isolation. Patients often found that their symptoms could influence each other. For example, a flare of pain and discomfort might also occur alongside fatigue. Furthermore, other factors such as stress could also influence these symptoms. Despite the fact that more than one symptom is often present at any one time, in the following sections for ease of presentation, I summarise the results of the focus group discussions on each of the individual symptoms of fatigue, sleep disturbances and pain. However, the overlapping nature of the symptoms is evident in the following sections.

5.2.1.2 The experience of fatigue

Fatigue was a symptom experienced regularly by all the patients in the focus groups. Some patients experienced fatigue as being ever-present, with flares of more severe fatigue. Others experienced fatigue intermittently, with periods of time when they had very little fatigue followed by flares of moderate and severe fatigue. However, flares of more severe fatigue could come on quite rapidly for all patients and I give an example of this at the end of the current section, in the context of physical fatigue.

During the discussions, participants described a clear distinction between ‘physical’ and ‘mental’ fatigue. These phenomena were experienced both simultaneously, or separately, as one patient explained:

PP3 I get, er, physical fatigue a lot ... during the day it'll come on. You mightn't have the mental fatigue at that time. (FG1B 96-109)

Mental fatigue was described as ‘*a great cloud kind of building up in your head*’ (PP7 FG1B 36-37) and as ‘*brain fog*’ (PP8 FG2B 350). For one patient in particular, mental fatigue was much more of a problem than physical fatigue and affected her concentration.

Consequently, it was sometimes difficult for her to achieve deadlines at work, such as written reports. Furthermore, mental fatigue, seemed to influence patients’ cognition which affected their perception of verbal expression and memory:

PP8 *[Sometimes] I just can't [think]. Some of the things I say are just ridiculous. ...*

AHM2 *She'll say something and deny saying it. If I pull her up and say, "You've said X, Y, and Z."*

PP8 *"You said so and so."*

AHM2 *"No I didn't." ... She did it the other day and my son was round and he says, "You did Mum." ... "You said that, Mum." (Laughter)*

PP8 *And, I, I don't realise I've done it or I, I forget things. (FG2B 360-378)*

Participants therefore regarded any cognitive difficulties they might have as being a consequence of their mental fatigue.

Physical fatigue was described very differently; as a heavy sensation *'like somebody's putting bags of potatoes on your body'* (PP3 FG1B 99-100) as though *'everything's weighing your down'* (PP3 FG1B 110-111). This sensation could strike quite suddenly, and when it was present, it felt like an effort to lift limbs or move. This sudden onset of a severe fatigue was also depicted as a sensation of being deflated:

PP9 *You just think someone had stuck a needle in me and drained.*

PP3 *Drained you, mhm.*

PP9 *Everything out of you. It just –*

PP3 *Like a vampire sucking the life out of you.*

PP7 *I just, sort of, just go limp. (FG3A 550-558)*

This sudden onset was a common experience amongst patients and it could be present for varying lengths of time. For one it often meant that he has to stop and rest; *'I get to a point where I've now just got to switch off'* (PP5 FG1B 733). After a while, however he felt able to continue again, but others were restricted for much longer periods, sometimes for several days. This severe fatigue was described as being *'overwhelming at times'* (PP3 FG1B 187). A patient's husband could identify when his wife was experiencing a sudden fatigue episode,

as he would observe the colour of her face changing to white. During those moments, she explained how she felt: *'I'm just like a rag doll'* (PP8 FG3A 575).

5.2.1.3 The consequences of fatigue on functional ability and participation

In general, the symptom of fatigue was a huge problem for patients as it *'dominates your life'* (PP3 FG1B 213) and consequently permeated all areas of their existence, including work, self-care, domestic, family and social activities of daily living.

First, fatigue had become a huge barrier to being able to 'do' many activities:

PP3 *I know you shouldn't allow it [to dictate your life], I know, but it's very hard when you want to do the things and you, you can't physically do them.* (FG1B 213-218)

Some had completely ruled out certain activities, as they felt physically unable to take part in them despite wanting to. Considering an activity, which consumes a lot of energy, was described felt like observing a huge mountain from its base:

PP6 *You're in the car park, you see all those other climbers go up. And your mind's saying, "Yes I can do that." But your body's just saying, "No."* (FG1B 285-287)

Physical fatigue seemed to affect functional mobility. One patient described how he could no longer keep the same pace as his wife if they were walking somewhere. Previously he said that he would have been the one who would be walking ahead. It was hard *'just getting your head round the mental fact you can't do it'* (PP1 FG1B 1538-1539) whenever they came across an activity that fatigue was preventing them from doing.

Participants considered fatigue as being the biggest factor preventing people with PSS from being able to engage fully in certain activities. However, one patient had been reflecting on her own reduced participation and had wondered whether it was her own *'inertia'* (PP4 FG1B 236) or reduced motivation which was preventing her from engaging fully. This view was not shared by others, who explained that they were motivated, but repeatedly were prevented from doing things due by their fatigue.

The mental fatigue described earlier, which could affect work productivity, also had implications for engagement even in some sedentary activities. A participant described strategies she had used to try and take her attention off her physical fatigue, but her mental fatigue prevented her distraction techniques from working:

PP3 You can't even concentrate on the TV to take your mind off it. ... You can't even read a book because if you read a book, I'll have read a, three chapters and think, "What the hell have I just written [read]?". And then if I'm watching the television, and I've done it many a time, I'll come to the end and I'll think, "Aye, what was all that about?". And it can be one of me favourite shows. (FG1B 115-130)

Therefore, instead of being able to redirect her attention from her physical fatigue to far less demanding activities, her focus was on her own reduced functional capacity.

Mental fatigue also had implications for activities requiring concentration. Consequently, some patients were reliant on others for certain things. One patient gave a description of how he now relied on his wife to sort out his medicines into a Dosette box, so he knows which medicines he needs to take when. His mental fatigue means that he is no longer able to attend to this task himself:

PP1 I mean I take- ... About 16 tablets a day. Now I can't put them up, I just, I, I haven't got the mental facility to, "I take one of them, and I take one, two of them. I take one of them." She sits on a Friday night for about two hours and puts all the tablets up for the week. (FG1B 1908-1915)

This participant was very aware his mental fatigue and reduced concentration meant his wife was taking on some caring responsibilities to support him. He regarded this as evidence of his decreasing independence.

The changeable nature of the fatigue also meant that arrangements often had to be changed or cancelled and this clearly affected others. A man whose wife has PSS described how the fatigue could put a stop to any plans that they both might have together:

AHM2 *With fatigue, when it gets to, say, four o'clock, five o'clock, and, and [my wife] wants to go out or we've planned to go out somewhere and she ends up in bed. There's nothing you can physi- you can do about it.* (FG2A 1382-1385)

Therefore, it was not just patients who regularly had to place their lives on pause, or frequently alter their plans; the lives of their spouses and their broader social networks had also become disrupted.

Since having a diagnosis and being aware of the limitations the fatigue has put on them, for some, part of their identity had changed. They had given up careers, hobbies and life roles due to the fatigue. One participant said *'I've never been someone with a weakness, I've been the sportsperson'* (PP5, FG1B 1711-1712). He was trying to deal with his altered identity and living with a symptom, which he saw as a *'weakness'*.

The effects of the fatigue meant that patients often found it a real effort to go out and engage in activities in the world and therefore began to feel socially isolated. Some had found that their world had become smaller. This social isolation was also due to *'the lack of understanding'* (PP7 FG1B 2073-2074) and *'because you are fighting this alone'* (PP7 FG1B 2084). When patients felt that they did not have understanding from other people, it could have a negative effect on their mood.

5.2.1.4 The experience of sleep disturbances

All patient participants reported experiencing sleep disturbances, which post-dated the onset of their PSS. A clear example of this is from someone who described being able to *'sleep on a washing line'* (PP7 FG1A 892) prior to developing her PSS. For her, getting off to sleep and staying asleep had been relatively effortless before PSS. After diagnosis however, she had perceived a reduction in sleep quality and an increase in the effort which she needed to put into falling asleep, such as ensuring her sleeping environment was right. This was a story to which other participants could also relate.

Some participants thought their disease caused their sleep problems and all believed that their sleep disturbance had become worse over time due to the effects of their PSS. In a

discussion where they considered why the disease might affect their sleep, one conclusion was that given that 'It's with you 24/7' (PP3 FG1A 754), it would naturally impact sleep.

PP3 *The thing is it affects you so much during the day, realistically when you think about it, why would it switch itself off at night when you went to bed to sleep?*

PP6 *Mhm.*

PP7 *Mhm.*

PP5 *Good point.*

PP3 *It doesn't go when you go to bed*

PP2 *No*

PP3 *The Sjögren's is still there, so it just obviously it manifests in a different way, which is not letting you sleep basically.*

PP2 *Yeah, that's it. (FG1A: 722-737)*

In this way, patients relied on their lay reasoning to make sense of the impact of the disease. For example, one person considered how her co-morbidities further contributed to her sleep difficulties, including her hypothyroid problems and the menopause.

PP6 *The thyroid's upset if the Sjogren's is upset and they'll upset each other. If I've got the flushes and the weird mood-swings and whatever's going on up here in the head; then I start having nightmares and disturbed sleep. (FG1A: 124-127)*

She also found that if one condition was symptomatic, it would affect her other conditions, such as her menopause or thyroid disease, causing a flare of those symptoms, resulting in further sleep difficulties and creating a vicious cycle.

However, the idea that sleep problems were somehow tied to PSS, was not an association that all patients had considered automatically. Furthermore, they had not been informed by health professionals about any potential impact on their sleep. As they noticed a change in sleep, they were left to ask *'What's going on? Is it to do with this mad crazy disease ...?'* (PP6 FG1A 165-166). One participant had previously reasoned her sleep disturbances were due to the ageing process:

PP4 *I've only recently, sort of, realised that ... [my sleep disturbance] actually might be Sjögren's related rather than age related (Laughter), which everything is when you get to my advanced years. (FG1A: 264-266)*

This patient had reached this conclusion after discovering an article about sleep and PSS on the internet.

We have just seen that sleep disturbances were common amongst participants since the onset of their disease. The specific types of sleep disturbances however, varied.

Unrefreshing sleep was commonly experienced and for one patient, even on the occasions she was able to sleep for 8-9 hours per night, it meant she would *'wake up and feel as if [she'd] never been to bed'* (PP4 FG1A 247). For someone else, it felt as though he had done a *'night shift as opposed to having a sleep'* (PP5 FG1A 449) due to feeling so exhausted when he woke up. This non-restorative sleep was seen as an *'emotional disappointment'* (PP7, FG1A 451) due to having an expectation of feeling refreshed in the morning, only to find that this need was not being met.

Difficulty with sleep onset was a distinct problem raised during focus group discussions. A participant explained that although occasionally he was able to get to sleep relatively quickly, he regularly struggled to initially get off to sleep. He described an example of what this meant for him in practical terms, from a couple of nights previously: *'I was lying awake at half past one thinking, "When am I going to go to sleep?"'* (PP5 FG1A 409-410).

Another form of sleep disturbance were regular night awakenings, which were a commonly experienced problem by patient participants. One lady often found herself awake for *'two to three hours'* (PP4 FG1A 257) in the middle of the night before falling asleep again and consequently would wake up feeling as though she had not slept at all. Similarly, another

participant would eventually doze off after waking during the night. However, she described the sleep she experienced following a long spell of lying in bed awake as *'not exactly sleep, sleep'* (PP7 FG1A 238) and that this (dozing) sleep was dissatisfying as it was perceived as being inferior to regular sleep. Another participant who regularly experienced night awakenings was usually able to fall back to sleep again but only to continue to wake frequently during the night such as *'at one, and half past two, and five'* (PP5 FG1A 1781).

Interestingly, one person shared how his problems were different to those described by other participants with PSS. He did not experience sleep onset difficulties or regular night awakenings. However, he regularly experienced what he considered a short sleep duration. *'If I get four hours sleep/five hours sleep a night I, I'll be lucky'* (PP1 FG1A 33). As well as experiencing a short sleep duration, he also gave the impression of an altered circadian rhythm as he both went to sleep and woke up very early.

PP1 *I mean I usually go to bed round half past seven/eight o'clock. And I'm up again at 1:00, and that's it. And I'm there, one o'clock and I'm there 'til half past seven the next; eight o'clock the next night. (PP1 FG1A 23-29)*

This had implications for his wife:

AHM1 *Unfortunately that, sort of, buggers me up for the day as well. (Laughter)*

Kate: *Yeah.*

AHM1 *'Cause he, he gets up, disturbs me. I don't go to bed at eight o'clock, I go to bed about half past ten/eleven o'clock, so after a couple of hours I've just got into a deep sleep and this one gets up. (FG1A 37-44)*

Patients' sleep disturbances did have consequences for bed partners. For one participant, it had meant *'I've thought about saying to my other half, "We'll have separate rooms", we already have separate beds'* (PP6 FG1A 116-118). The impact of poor sleep on relationships was not explored in detail, but the possible implications of poor sleep on relationships are clear.

A range of sleep problems were reported by participants and they also described that although they may experience one particular sleep problem at one time, these can change. For example, a particular problem, such as difficulty with sleep onset, may not consistently be present, but it can be replaced by another sleep disturbance instead. One participant explained how this played out for him:

PP5 It's just an inconsistent thing with me, other nights I can fall asleep virtually as soon as I put my head on the pillow, but then wake up several times during the night. (FG1A 421-423)

Another lady frequently experienced inconsistency in her sleep and no longer took for granted a full night's sleep.

PP2 I still have erratic sleep pattern. ... I can go to bed at 11 o'clock and not get to sleep at all. ... I can go to bed at 11 o'clock and sleep until about 2, and that's it. ... And occasionally, very, very, very occasionally I sleep right through, and that's always something to look forward to. (FG1A 67-80)

When she did occasionally experience a good night's sleep, this was very satisfying and somewhat of a relief.

Patients explained that other symptoms influenced their sleep. Pain was a factor, which occasionally seemed to disrupt sleep; however, it was unclear whether this specifically related to PSS or to other comorbid musculoskeletal problems:

PP10 Two nights ago I never slept all night 'cause of the [neck] pain and it had, it went down me arms and me hands. (FG3A 193-4)

Discomfort relating to dryness seemed to have a greater impact on sleep than pain. Oral and ocular dryness in particular caused a huge amount of discomfort for some people and they felt the dryness was responsible at times for waking them in the night:

PP3 I really struggle with the dryness in my eyes and my mouth during the night. ... I wake up like three or four times, like somebody's put a hairdryer in your mouth. ... And sometimes it catches your throat and you can wake

yourself up trying to swallow. ... It's a horrible feeling. And as much as you try to get a glass of water, a second later it's still like you've been in the desert. ... And then the dryness, I put Lacri-lube in my eyes, and I can put it in three or four times during the night and I'll still wake up like they've got sand in them. (FG1A 294-315)

It is entirely possible that someone waking to use the toilet during the night could be more attentive to their dryness symptoms once they have woken up, rather than it being the cause of their waking. However, participants did not raise this scenario and they concluded that the dryness had been the factor, which had disturbed their sleep.

Discomfort in the legs was another factor, which participants said, could interfere with sleep. The various types of leg discomfort described, related specifically to poor peripheral circulation and reduced sensation. The specific discomfort of cold legs during the night was shared by several participations:

PP3 I get discomfort in my legs 'cause I have bad circulation. I've thermals on in the summer all the time.

PP1 Yeah, yeah.

PP3 My friends laugh, it's crazy, I can't keep the heat in my legs. Erm, I've got an electric blanket as well which does help. But it's, I get a lot of discomfort in bed until I actually get off, erm, to sleep and stuff. And, er, erm, but it's more so in my legs I get the discomfort. (FG1A 939-947)

Sleep disturbances did have consequences for other PSS symptoms, making them seem worse. Fatigue was a natural consequence of poor sleep, which meant the ability to participate and perform daily activities was restricted.

PP4 Yes, you could see, erm, sort of, link too isn't there between disturbed sleep or inadequate sleep and fatigue the next day so you can't do the things you want to do during the day.

PP1 *Mhm yeah.*

PP4 *And you wander about like a zombie. (FG1A 764-766)*

Unsurprisingly, another impact of sleep disturbances was daytime sleepiness. The wife of a patient described how she regularly observed her husband falling asleep inadvertently during the day:

AHM1 *And he'll be sitting on a chair and then I'll be talking to him and I'll, "Are you listening?" and he's asleep (Laughter), you know, during the day he's nodded off 10 minutes, and I'm talking away to meself. (FG1A 558-560)*

Other participants also regularly experienced falling asleep during the day, for example while sitting down to watch television in the afternoon. However, inadvertently falling asleep during the day, whilst in the company of other people could be embarrassing at times.

PP5 *I was actually at a friend's yesterday afternoon, we're chatting, and I actually fell asleep. (Laughter).*

PP8 *Mid-conversation?*

PP5 *Yeah, literally, almost. (Laughter).*

PP8 *I've done that. (FG3A 975-982)*

Another participant fell asleep during one of the focus group discussions despite being actively involved in the discussion before and after she dozed off. Daytime sleepiness, was therefore, both observed and described as being a real problem, which impacted on patients' daily function and participation.

It was felt that sleep disturbance resulted in an increase in fatigue, but that fatigue also led to daytime sleepiness. However frustratingly for participants with PSS, fatigue did not always lead to sleep at night, and one participant highlighted a reason for this paradox was because '*the fatigue is a different thing to tiredness*' (FG1A, PP3, 392).

Sleep was regarded as a precious resource. It was something that people no longer took for granted. It was also considered a linchpin, in the fact that it was seen as a strong influencing factor on other symptoms such as fatigue and depression:

PP4 If that one's wrong [sleep] a lot of the other ones'll fall. I suppose it's like ... the domino theory'. (FG1 821-822)

If they did not sleep well, patient participants would feel fatigued, consequently feel low in mood and experience more worry.

5.2.1.5 The experience of pain and discomfort

Although pain was a priority symptom identified within the concept mapping study (see Chapter 3, it was not immediately a term which patients fully related to in the discussions. They explained; '*It's a funny one. Pain? Discomfort?*' (PP6, FG3B 18); '*It isn't pain pure and simple*' (PP7 FG3B 24). There was a strong feeling that the word '*pain*' was not always an adequate term for the broad spectrum of symptoms they believed that this word was supposed to cover. First of all this phenomenon was experienced '*on a sliding scale*' (PP7, FG3A 20):

PP7 It can be anything from a mild irritation, as it were, right the way through to absolutely excruciating. (FG3A 28-29)

Patients used the descriptive terms '*irritation*' and '*discomfort*' for what they experienced at the lower end of this spectrum. Further up the scale, they might experience '*a nagging pain ... aching pain*' (PP5 FG3B 947) and at the top end was severe pain. It also became clear during the discussions that some participants preferred the term discomfort to pain, as they were better able to relate to it. Some peoples' experiences of pain only went so far up the spectrum as they tended to live with discomfort and not pain. One person did not relate to having pain at all, in the context of her PSS. She considered pain in the context of a previous biomechanical injury:

PP8 I don't have the pain. I mean I've had discs out of my back so, I mean, I know what pain is. (FG3A 936-937)

Location of the pain and discomfort was an additional factor, which influenced how it patients described it:

PP7 Well for me it depends on A) where it is. ... So, for example, my eyes are rarely what I would describe as painful. But they're very often extremely uncomfortable. ... Whereas my neck... And the, and the arthritic bits are extremely painful when they flare up.

PP9 That's a good point actually. (FG3B 37-50)

The discussions demonstrated that the experiences of pain and discomfort were diverse between individuals. Pain was not a symptom which was present for everyone, or that was present for all the time. In those who did have pain their experience varied. When pain was present it could vary, both in location and severity.

Some patients described having joint pain in different areas of their bodies, particularly in upper limbs and spine. One patient said she was '*in constant pain*' (PP10 FG3A 187) in her neck, and another said she often had pain in her hands, wrists and elbows. A spouse of a patient thought that the articular pain people were describing was due to having arthritis rather than PSS:

AHM2 I think the pain's possibly might be to do with the arthritis side of it rather than the Sjögren's, ... the Sjögren's is more discomfort. (FG3A 72-73)

It is possible that people were describing pain from co-morbid arthritis, but despite its cause, articular pain was present in several patients and this pain was viewed as '*proper pain*' (PP7 FG3A 921) on the irritation/pain spectrum. One person also explained how her neck pain was worse during bad weather because '*when it's good [the weather] it's not too bad [the pain]*' (PP10 FG3A 198).

Headaches were another type of pain which were commonly experienced amongst participants. The type of headaches varied between individuals but there were some similarities in the pain distribution for some people:

PP9 I get a headache here that goes down into the neck.

PP7 Yes.

PP9 And then along the shoulder.

PP7 I get that as well. (FG3A 1231-1237)

Some people's headaches were more localised such as '*at the top of the head*' (PP10 FG3A 1245) and '*behind my left eye*' (PP5 FG3A 1250).

Peripheral tingling sensations, particularly in the hands and feet were present for some patients. Although this seemed to be an unpleasant sensation as '*sometimes it's quite numb*' (PP6 FG3A 1314); no-one identified it as being painful. It could occur during activity and without warning; '*all of a sudden it comes. It, it's peculiar*' (PP6 FG3A 1330). This particular patient explained how she had previously been investigated for multiple sclerosis prior to her PSS diagnosis because of her tingling sensations.

Gastrointestinal symptoms were another type of discomfort raised during the discussions. For example, nausea sometimes accompanied headaches. Furthermore, bowel pain, discomfort and occasional lack of control were a further problem for some people. Several patients experienced both nausea and discomfort in their abdominal region when they were feeling particularly fatigued. These sensations could affect their appetite:

PP9 If you've got that nausea feeling it just feels as if you're hollow inside and, erm...

PP3 Yeah, it's like an empty feeling isn't it? Yes.

PP9 Yes, it's, it, I don't know whether that's pain or a deep ache or... But it's, erm, it's when you're really tired. ... And, erm, probably pushed too hard. ... And, erm, you just feel nauseous and you don't fancy to, anything to eat. (FG3A 326-345)

Nausea, in addition to being present alongside fatigue, could manifest quite suddenly and be accompanied by a heavy sensation '*like you've been at the gym for the full day. ... like, er,*

you've done a marathon' (PP3 FG3A 352-356). However, it did not necessarily follow exercise. Other patients could relate to this diffuse, heavy feeling:

PP6 *I sometimes feel like somebody's poured lead. I always say to me GP, it's my legs, right at the tops of me legs. ... And it's like somebody's poured lead into the legs and they've very heavy and it feels as if you're walking through treacle.* (FG3A 984-994)

Following a fatigue episode, another patient described how initially the nausea would start, followed by joint pain:

PP3 *When my fatigue comes on and I feel like really heavy, and to me it's like a sickly feeling. I get like a sickly heavy- ... A sickly heaviness like a- ... like a, just like a nausea feeling comes over you. ... That's what I get. And then these start to burn, the joints and the wrists.* (FG3A 242-257)

For the patient participants, the combined unpleasant experiences of nausea and widespread discomfort and pain rarely occurred in isolation, but would often manifest themselves following the onset of a sudden extreme fatigue episode.

Pain and discomfort associated with dryness was another common problem. As has already been mentioned, discomfort was the term which was seen as a more accurate description for the sensations associated with dry eyes.

Oral dryness seemed to result in very specific types of pain and discomfort as one lady explained:

PP9 *I mean my dentistry history has been terrible, you know, I've had them all filled and capped and then recapped.*

PP8 *Oh mine is the same, yes.*

PP9 *And then extracted. So now I've got, er, dentures. Top one's fine 'cause there's a bit of suction, bottom one just floats 'cause I've got no gum and ... it's not pain exactly but it's certainly discomfort. And there has*

been a lot of pain, when I had extractions and things like that. ... So there is that level of pain there, which everybody would have with having extractions and caps and recaps... dentistry is, erm, it's a, it's a well-known thing, I mean, er, er, from the fact of being a Sjögren's [patient] because your mouth is so very dry. (FG3A 118-141)

Oral dryness creates an ideal climate for tooth decay, gum disease and tooth loss. The dryness had resulted in dental work being necessary for some of the participants. These dental treatments could be very painful.

Another very specific pain, experienced in the mouth area, was a severe cramp-like pain in the parotid glands:

PP7 When this flares up- (pointing to side of face). ... Wow, that is the end.

PP6 Yes, yes.

PP10 Yes, it's so sore.

PP9 Yes, mine's here. (Pointing to salivary glands on side of face)

PP7 It's absolutely excruciating, there's no other word for it. ... And you get like a spasm and it all comes right out here.

PP3 It goes rock hard.

PP7 It does. And it's so, so, so, so painful.

PP3 I get that. ... It doesn't last does it?

PP7 No, it doesn't take long. ...

PP9 About four/five minutes.

PP3 It's really painful isn't it?

PP9 *Yeah.* (FG3A 1639-1716)

Although this pain occurs temporarily for short periods, it is severe when it strikes and most unpleasant. Discussing this shared experience seemed to be important to those involved in the above conversation. For some it was the first time they had been able to talk about this particular sensation with others who had first-hand experience of the same phenomenon.

A further presentation of discomfort was the inability to tolerate particular sounds or loud noises as someone explained:

PP6 *And I love music ... there are certain things that I've loved from, you know, since I was knee-high to the grasshopper. And then there's certain times when the noise stimulus is just too much. And I think that's peculiar.*
(FG3A 779-780)

This person, who had always enjoyed playing her music, had found that at times she was unable to listen to it and enjoy it, now she is living with PSS. Intolerance to noise was a problem, which several of the patients experienced, but this occurred intermittently; it was not a constant state.

Intolerance to light was another sensory disturbance affecting one patient. She described having to close her eyes in natural light and consequently either always sunglasses or glasses with lenses which react to light.

From the above descriptions of pain and discomfort experienced by PSS patients, it can be seen that the presentation of these symptoms in PSS is heterogeneous and that these symptoms can vary considerably both within and between patients. The sliding scale of pain described by participants, with specific examples along the continuum can be seen in Figure 5:1.

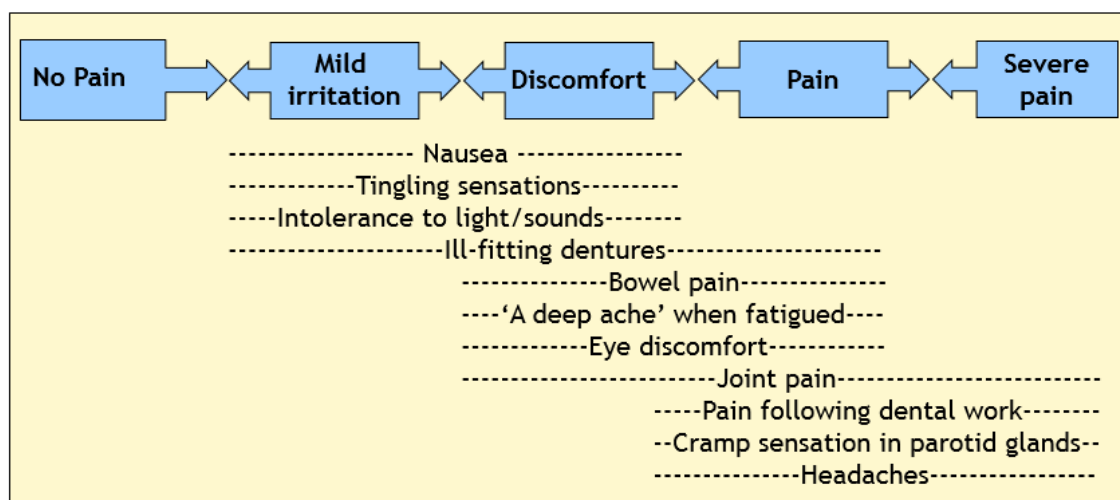


Figure 5:1 The sliding scale of pain with specific examples along the continuum

5.3 Discussion

The focus group discussions revealed that fatigue, sleep disturbances and pain and discomfort were all experienced by PSS patient participants. Furthermore, these symptoms greatly impacted on their lives and those of their family members. Problems encountered by patients, resulting from their symptoms included increased social isolation, reduced ability to perform physical and mental activities and the sense that they were misunderstood by those around them. All of these factors could impact upon mood. There was an overlap of symptoms and one symptom often seemed to affect another. For this reason, it was sometimes difficult for participants to discuss one symptom in isolation. Furthermore, symptoms were not always present and could vary. 'Symptom complexes' are not unique to PSS and the interactions of symptoms and their palindromic nature have been previously described in seropositive and early rheumatoid arthritis patients (Stack *et al.*, 2013; Stack *et al.*, 2014).

Participants found it particularly useful to discuss their individual experiences with others. Although the focus groups were not designed to be therapeutic in any way, patients reported that it was helpful to be able to share experiences and talk through specific difficulties with others who understood. Patients with rheumatic diseases (including PSS) who took part in another qualitative study investigating the impact of written fatigue

information similarly, found the qualitative interview process itself to be therapeutic, despite it not being intended that way (Hart *et al.*, 2016).

It is essential that symptoms are believed and acknowledged by HCPs during appointments and that they are not easily written off, for example as a symptom of old age, as this can be devastating to patients. In the general population fatigue may be more prevalent in older age groups (Avlund, 2010). However in PSS, increased fatigue is actually associated with younger age (Overman *et al.*, 2016). HCPs can often feel reluctant to dwell on a symptom, particularly fatigue when they are not certain of its aetiology or available treatments (Repping-Wuts *et al.*, 2008). Educating HCPs about PSS, its symptoms and their management would therefore be of benefit to patients, if it resulted in more understanding clinicians.

Mental fatigue was an aspect of fatigue which was discussed. Participants described some symptoms of cognitive impairment, which included difficulties with concentration and poor memory. These cognitive symptoms are a known problem in PSS patients (Segal *et al.*, 2012; Blanc *et al.*, 2013) and although patients did not perceive them to be constant, they did affect their ability to fully engage in some daily activities. Although patients explained mental fatigue could occur in isolation, they described it often occurring with physical fatigue, or following an episode of over-exertion. The experience of both physical and mental fatigue taking place together, has been reported previously in qualitative studies of other fatiguing conditions, including chronic fatigue syndrome (Keech *et al.*, 2015) and fibromyalgia (Stamm *et al.*, 2014).

Physical fatigue was described as a distinct heavy feeling which could strike suddenly and at times was overwhelming. The sudden onset of fatigue (which was sometimes accompanied with pain) is similar to the '*boom and crash*' pattern described in a qualitative study of CFS/ME patients (Pemberton and Cox, 2014). During the crash phase, usual activity had to stop.

Levels of fatigue were both variable, often unpredictable and at times overwhelming. Similar qualitative findings have likewise been reported in other arthritic conditions including RA (Hewlett *et al.*, 2005), fibromyalgia (Vincent *et al.*, 2016) and SLE (Connolly *et al.*, 2014).

Fatigue had far reaching implications for people's lives. Focus group participants had been forced to give up careers and roles and had placed their lives on pause because of it. This biographical disruption was identified in the literature many years ago, following the onset of a chronic disease and its associated symptoms (Bury, 1982). This study also raised the issue that life was often interrupted with smaller intermittent pauses during a flare of fatigue, where it became necessary to stop activity. This is similar to the consequence of fatigue in both RA and SLE patients (McElhone *et al.*, 2010; Thomsen *et al.*, 2015) and affected others. Social isolation was also raised as a problem, which was a consequence of fatigue. Social isolation in people who develop a chronic illness has previously been discussed in the literature and is in part due to the impact of an illness disrupting previous life roles (Bury, 1982; Charmaz, 1983).

Motivation was a concern for one participant who experienced fatigue regularly, particularly during poor weather. Reduced motivation is a symptom of low mood and depression, which has an increased prevalence in PSS (Valtysdottir *et al.*, 2000; Harboe *et al.*, 2009; Kotsis *et al.*, 2014). Furthermore, depression is a predictor of PSS fatigue and if identified, should be addressed in clinical settings (Karageorgas *et al.*, 2016).

Sleep disturbances were evident amongst the PSS participants during the focus groups. Sleep disturbances are seen in a range of chronic diseases (Kamath *et al.*, 2015) and there are broad similarities between the sleep difficulties experienced in PSS and in other conditions such as primary insomnia (Frankel *et al.*, 1976; Reynolds *et al.*, 1991), fibromyalgia (Katic *et al.*, 2015) and chronic pain (Tang *et al.*, 2015). Not all participants had made an association with their sleep disturbances and their PSS. This is possibly due to the prevalence of sleep disturbances until recently, being relatively under-recognised in PSS (Hackett *et al.*, 2016a).

Participants perceived that some of their other symptoms interrupted their sleep, including pain, discomfort and dryness. The specific types of sleep difficulties they experience have recently been summarised in the PSS literature (Hackett *et al.*, 2016a). They include problems with sleep onset, night awakenings, altered circadian rhythm, dryness, and short sleep duration (Gudbjornsson *et al.*, 1993; Hay and Morton, 2006; Hilditch *et al.*, 2008; Theander *et al.*, 2010; Usmani *et al.*, 2012; Hackett *et al.*, 2016a). In this study, patients' leg discomfort and altered sensation were specific symptoms interfering with sleep. It is

possible that these may be due to peripheral neuropathy or restless leg syndrome, which both occur within PSS populations (Hening and Caivano, 2008; Carvajal Alegria *et al.*, 2016). It is essential that the specific problems are picked up in a consultation as the individual treatment modalities for each may vary. For example restless legs syndrome may be successfully treated pharmacologically with dopaminergic therapies (Zak and Walters, 2015). Furthermore, if a primary sleep disorder is suspected (such as obstructive sleep apnoea), patients should be referred to the appropriate specialist for further investigations (Hackett *et al.*, 2016a).

Night awakenings were a particular problem, occurring alongside dryness and discomfort. Furthermore, sleep onset difficulties were identified by several focus group members. Both these problems are symptoms of insomnia and as such, should be amenable to CBT-I (Trauer *et al.*, 2015). However, due to the unique feature of oral and ocular dryness also interfering with sleep in PSS, a dryness management component may form a useful adjunct to a CBT-I intervention.

Participants in this study described an overlap between their sleep and fatigue symptoms. This is neither surprising nor unique to PSS, as this overlap is recognised in both primary insomnia and in other fatiguing conditions (Buysse, 2013; Brass *et al.*, 2014; Gotts *et al.*, 2016). Furthermore, participants saw sleep as a precious resource, which, if disrupted resulted in an exacerbation of their other symptoms. It therefore makes sense that sleep could be appropriate symptom target, and if successfully treated, might have a positive influence on other symptoms, including fatigue, anxiety, depression and pain (Thorndike *et al.*, 2013; Tang *et al.*, 2015).

Although patients recognised pain as being a symptom of their PSS, not all had it. Furthermore, the term '*pain*' was not necessarily regarded as being appropriate to describe the symptom and should be used interchangeably with the term '*discomfort*'. The terms pain and discomfort covered a range of experiences and symptoms which could be viewed on a sliding scale.

The gastrointestinal symptoms may be related to irritable bowel syndrome (Bengtsson *et al.*, 2011) or other complications such as dysautonomia (Newton *et al.*, 2012). These features may require a coordinated approach, with the involvement of an appropriate

clinician. Headaches were also identified in this study. A previous study demonstrated an increased prevalence of headaches in PSS patients compared with healthy controls (Tjensvoll *et al.*, 2014). An intolerance of light and noise by some participants was also a problem for some. These features are also described in fibromyalgia and CFS (Soderlund *et al.*, 2000; Meeus and Nijs, 2007; Clauw, 2014).

Little is known about pain in PSS. In one cross-sectional study of 100 PSS patients, fibromyalgia was identified in 31 individuals (Choi *et al.*, 2016) using the American College of Rheumatology (ACR) 2010 Criteria (Wolfe *et al.*, 2010). This is much greater than the 5% prevalence of fibromyalgia (determined using the same criteria) in the general population (Vincent *et al.*, 2013). The characteristics of fibromyalgia identified by Clauw (2014) can be seen in Table 5-4. There are many similarities between these characteristics and symptoms described by patients during the focus groups. Fibromyalgia has been described as a centralised pain state (Clauw, 2014). The pain is regarded as being centralised as it is assumed to relate to a dysfunction of the central nervous system or pathology which contributes to both the development and the maintenance of chronic pain (Williams and Clauw, 2009; Phillips and Clauw, 2013).

Characteristics of Fibromyalgia and other centralised pain syndromes
<p>Character and quality of pain</p> <ul style="list-style-type: none"> • Diffuse or multifocal, often waxes and wanes, and is frequently migratory in nature • Often accompanied by dysesthesia or paraesthesia's and described as more "neuropathic" (e.g., with terms such as numbness, tingling, burning) • Patients may note discomfort when they are touched or when wearing tight clothing <p>History of pain in other body regions earlier in life</p> <p>Accompanying comorbid symptoms also of central nervous system origin</p> <ul style="list-style-type: none"> • Often fatigue , sleep disturbances, memory, and mood difficulties accompany centralized pain states such as fibromyalgia • Several of these symptoms will typically improve along with pain when individuals are successfully treated with appropriate pharmacological or nonpharmacological therapies <p>Symptoms suggesting more global sensory hyper-responsiveness</p> <ul style="list-style-type: none"> • Sensitivity to bright lights, loud noises, and odours and even many visceral (autonomic) symptoms may be in part due to a global sensory hyper-responsiveness seen in conditions such as fibromyalgia

Table 5-4 Characteristics of fibromyalgia and other centralised pain syndromes (adapted from Clauw, 2014)

The term '*fibromyalgianess*' has been coined to describe a spectrum of the intensity of, or sensitivity to, fibromyalgia symptoms which was identified in RA patients in response to completing a symptom questionnaire (Wolfe, 2009). At one end of the spectrum, no fibromyalgia symptoms are evident, whereas at the other end, a person may experience high levels of all symptoms. The spectrum highlights the problem of dichotomising patients into having a diagnosis of fibromyalgia or not, as many people are likely to score somewhere between both extremes of the scale, therefore experiencing a level of fibromyalgianess (Wolfe, 2009). The discordance between subjective and objective symptom scores in PSS

has been highlighted by a group in Newcastle previously (Robinson *et al.*, 2014), and pain centralisation in some patients may be one possible explanation for this discordance.

Due to the range of experiences associated with the term pain, standard measures used in clinics (such as a pain VAS), may not pick up all the details. Therefore, appropriate measurement is needed in order to identify the specific issues of pain and discomfort and their severity as this may help guide clinicians towards appropriate interventions.

Pain and discomfort levels were variable between and within participants. Patients also made their own association with pain and fatigue. The Newcastle group has recently highlighted the close association of these symptoms in a large cohort study of UK patients. This study identified four specific phenotypes of PSS patients and was further validated in two international cohorts (Lendrem *et al.*, 2016). Patients who experienced pain, also experienced fatigue and these patients were likely to belong to two out of four clinical phenotypes; specifically, the 'high symptom burden' group and the 'low anxiety and depression' group. Therefore, PSS patients who experience pain or fatigue, may benefit from different clinical management from those who do not. However, this study has suggested that patients perceive that their pain is often worse following a period of raised activity levels. Therefore, the implementation of fatigue activity management strategies such as problem solving, planning, prioritising and pacing (Arthritis Research UK, 2011), may also support with pain management.

There are several limitations to this focus group study. The focus groups were conducted during a weekday morning from a convenience sample of a relatively small number of patients. This meant that none of the PSS group members worked full-time and some useful insights may have been missed. However, there was representation from patients and family members who worked part-time, were unemployed and were retired. This study discussed several symptoms in depth and was conducted with people who had a lived experience of the symptoms. Finally, the participants were recruited from a North East clinic and as such some insights might have been missed from patients from different regions.

5.4 Summary

This chapter has described both methods and results from focus group discussions with PSS patients and spouses of patients about symptoms of fatigue, sleep disturbances and pain. In the following chapter, I discuss further results from the focus group discussions, including the types of self-help strategies patients have found useful for managing these symptoms. Furthermore, I present feedback from patients about intervention components which were suggested by clinicians (in Section 4.4.2.) and report participants' thoughts and reactions to potential modes of delivering future symptom management interventions.

Chapter 6. Developing a new care package for PSS symptoms: A qualitative study

In the previous chapter, I described how I conducted focus groups with PSS patients and family members to explore the symptoms of fatigue, sleep disturbances and pain in more detail. In this chapter, I present further results from the same qualitative focus groups. Firstly, I describe the strategies patients have implemented to self-manage these symptoms. Secondly, I describe their responses to the interventions proposed during the previous clinician validation process (in Chapter 4). Finally, I describe a model of delivering future symptom management following feedback from patient and family stakeholders in this focus group study.

6.1 Method

6.1.1 Aims

- To determine which strategies patients use to manage their symptoms of fatigue, sleep disturbances and pain and discomfort.
- To explore the acceptability of potential intervention components with patients and their family members.

The focus groups and analysis were conducted in the same way as described in Chapter Chapter 5 (Section 5.1). The specific items covered in this aspect of the study are reported in the topic guide (Table 6-1). Each of these items was presented to participants on sheets of paper during the focus groups with space for participants to jot down any written responses onto the handouts if they wished. These were separated out for each topic. For example, when the topic of sleep disturbances were discussed, the handouts only included questions on sleep and possible intervention components to help manage sleep disturbances. Similarly, when the handout materials for the fatigue focus groups only included questions and intervention components relating to this topic. The same was true for the pain topic. The intervention strategies were explained by myself and Dr Deary, the focus group co-facilitator.

Topic guide
<p>How do you (or your relative) currently manage your:</p> <ul style="list-style-type: none"> • Fatigue? • Sleep difficulties? • Pain? <p>Here are some possible non-drug intervention solutions. What do you think about each?</p>
Fatigue (a brief verbal description was given of each strategy or approach):
<p>Cognitive behavioural therapy (CBT)</p> <p>Pacing</p> <p>Planning</p> <p>Prioritising</p> <p>Delegating</p> <p>Strength/balance exercises</p> <p>Gradually increasing physical activity/grading exercise</p> <p>Online course/therapy</p> <p>Individual therapy with a health care professional</p> <p>Group fatigue management programme</p>
Sleep (a brief verbal description was given of each strategy or approach):
<p>Cognitive behavioural therapy for insomnia (CBT-I)</p> <p>Establishing a bedtime wind-down routine</p> <p>Removing all activities such as computers/crafts/books from the bed</p> <p>Restricting time spent in bed</p> <p>Keeping a record of sleep in a sleep diary</p> <p>Talking through any unhelpful thoughts about sleep with a healthcare professional</p> <p>Getting up after 15 minutes if haven't managed to fall asleep</p> <p>Online course/therapy</p> <p>Having 6 individual therapy appointments with a health-care professional</p>
Pain (a brief verbal description was given of each strategy or approach):
<p>CBT</p> <p>Acceptance and commitment therapy</p> <p>Pacing or balancing activities with rest</p> <p>Increasing activity gradually</p> <p>Identifying unhelpful thoughts about pain</p> <p>Doing daily targeted exercises prescribed by a physiotherapist</p> <p>Taking part in an exercise group</p> <p>Using meditation or relaxation techniques</p> <p>Understanding more about why and how we experience pain (education)</p> <p>Doing an online course to help with managing pain</p> <p>Having some individual appointments with a health-care professional for specific support with pain management</p> <p>Attending a group to share experiences of managing pain with other people who have Sjögren's</p>

Table 6-1 Topic guide for intervention focus group discussion and modes of delivering interventions in the future

6.2 Results

6.2.1 Strategies currently used by patients to manage their fatigue, sleep disturbances and pain

A variety of strategies were utilised by participants to manage their symptoms. Many were adopted through trial and error and they generally continued to use those which provided benefit. However, not all strategies were helpful or necessarily received a positive response from friends, family or others, yet patients continued to use them. The strategies described by participants are discussed separately for each of the symptoms of fatigue, sleep disturbances and pain in the following sections. This is followed by a short section where I show how patients manage several symptoms collectively.

6.2.1.1 Strategies used to manage the symptom of fatigue

A variety of strategies were used to try to manage fatigue. Through accepting some help from others, one patient had succeeded in maintaining a previous role. He enjoyed being part of a local brass band. However, his fatigue meant that it was too much physical effort for him to carry his own heavy instrument, meaning he regularly received some assistance from another band member.

PP1 I play a tuba in a brass band, I can still play it but I can't carry it. But it's never stopped us. I'm always getting one of the lads to, to hump the instrument around for us and I'll sit and I'll play it all day. (FG1B 477-486)

Through accepting help, he was able to continue with an activity which he enjoyed and which was important for his well-being.

Some participants felt that they did not want to be beaten by their disease or their fatigue. In effect despite feeling *'totally inert and you can't even get up out of a chair or even pick up a cup of, a cup of tea'* (FG1B 174-175), they had pushed themselves to continue doing things. There was a sense that living was a daily battle which *'at the end of the day you either give into it or you don't'* (PP1 FG1B 466). In this way, fatigue imposed restrictions, which could be difficult to accept. The friends of one patient had advised her to listen to her body and accept its limitations. However, she did not want to admit defeat:

PP6 *You're thinking, "Look, I'm not old." I'd accept, if I was 93 or something (Laughter) I'd be like, "Okay." I'd accept that. (FG1B 411-412)*

However, this strategy of constantly fighting the fatigue did not always end with positive results. If they pushed themselves to continue an activity, it could result in an exacerbation of symptoms at a later point.

PP2 *And sometimes you force yourself to do things. ... And then you suffer for it afterwards. (FG1B 161-167)*

A specific example was given when choosing to continue with physical exercise despite experiencing excessive fatigue. This could result in a '*detrimental effect*' (PP1 FG1B 1060) with even worse symptoms following the period of over exertion.

Medication was another strategy used by some patients to try and alleviate their fatigue. One participant talked about her experiences of the drug hydroxychloroquine: '*It does help with my fatigue, but it doesn't eradicate it, doesn't take it away*' (PP3 FG1B 664-665). Overall, the effects of this drug (which is commonly prescribed to PSS patients), were perceived as being minimal by those who had experience of taking it.

Several people had tried alternative medicines to help with fatigue including Shiatsu, which one patient believed had helped her mental fatigue.

PP7 *I have to say, that the Shiatsu has put me to pre-Sjögren's levels of concentration normally, in a normal day-to-day basis. And, and, and that mental clarity that I had before is there most of the time. ... And it, it's been a lifesaver. (FG1B 47-60)*

Several others had tried acupuncture and homeopathy but were less convinced about it having a positive impact on their fatigue symptoms. A further participant had searched for answers to his fatigue and investigated possible remedies which might help, but he said '*I haven't found anything [that helps] to be perfectly honest*' (PP5 FG1B 988).

Despite having significant problems with fatigue, patients were reluctant to seek help from, and talk about it with their general practitioners (GPs). Generally, there was a perception amongst group participants that GPs did not understand this symptom:

PP2 I've brought it up [the topic of fatigue with a GP] and I just read a blank stare. ... They don't, they don't understand.

PP7 They don't get it.

PP2 No.

PP1 And-

PP2 You just, you just can't get through. (FG1B 600-616)

Although another participant mentioned that she would talk to her GP about her painful joints; when I asked her if she had mentioned her fatigue to her doctor she replied; '*no, I just wouldn't*' (PP4 FG1A 594). This was because she felt that her GP had previously blamed some of her other symptoms, including her pain and poor sleep down to ageing. Fatigue was a huge symptom to her and the prospect of having this symptom, which was a dominant factor in her life, dismissed as a sign of old age, was enough to avoid mentioning it altogether.

Patients did not only avoid discussing their fatigue with health care professionals. Some also described keeping it from many people they came in regular contact with in their daily lives. The invisible nature of this symptom (described earlier in Section 5.2.1.1) was a barrier to talking about their fatigue. One patient felt it was necessary for her to present herself in a certain way to others, which in itself was exhausting:

PP6 I've got to look healthy and look fine ... You put the face on. ... It's like you, you, you, you're wearing a mask ... And you get sick and tired of wearing the mask. (FG1B 1632-1641)

Due to the negative responses this person had previously experienced from her family regarding her fatigue, she worked extra hard to keep it hidden from them, possibly to avoid further negative reactions.

However, hiding fatigue from others could create additional problems, including raised expectations in others. This could result in feeling as if *'you're being pushed all the time'* (PP2 FG1B 1768). Some thought that it would be helpful for others to know more about the disease and the specific symptoms, in particular, fatigue. However, as they found it difficult to explain the impact of their fatigue, a suggestion was made that some appropriately written information, or a booklet describing PSS and fatigue might help. One patient said she had come across a book which was simply written with illustrations which described chronic fatigue syndrome (CFS) to people who did not have CFS:

PP6 *And I flicked through the preview and I thought, "It's such a good idea" but just to say to people, or your boss or whatever, to say, "Look, this is how I feel. It's not a, a good night's sleep will not cure all." (FG1A 776-779)*

There was a sense that patients would feel empowered by something as simple as having appropriately written information to give to others, which would eliminate the pressure of them verbally trying to explain it, every time someone asked.

One participant had previously undertaken a course of CBT for her chronic pain. She found that it had equipped her with useful strategies, which she now used to pace her daily activities in order to minimise the effects of her fatigue. She described how the therapy had provided her with an ability to examine patterns in her life and to consider how these might interact with her physical symptoms, such as fatigue. One such strategy was to use a visual cue:

PP6 *I have an egg cup on the mantelpiece at home, which is one of me prompts, and it was, she [her CBT therapist] taught us to say, "That's your egg cup" she put it on, on the mantelpiece, "That is my energy for today. How are you going to use that energy effectively?" ... And I found that was a good, 'cause I like, I think visually and I like that prop... And*

thinking, “Right [participant's own name], if you drain the egg cup by 10 o’clock in the morning don’t be surprised if you’re, you’re crashed out.

Vincent Yeah, okay. So that helped you manage your energy?

PP6 Yes. (FG1B 1189-1205)

Following the completion of her CBT intervention, she also continued to keep a diary of her symptoms as she considered it to be a useful tool to help her map what was going on in her life; not only her pain, but also flares of her comorbidities, daily events and her fatigue.

For the purpose of the group discussion, pacing was described by the facilitators as dividing up activities/tasks, into smaller, bite-sized chunks and interspersing them with rest. Another patient had applied pacing techniques herself without the support of a health care professional and through doing this was successfully able to continue with the hobbies she found enjoyable, including gardening.

PP10 I do a bit of gardening. I do five minutes and then I have to sit down.

PP6 And then stop, yes.

PP10 And things, and then get up and do another five. But I have, if I pace meself it’s great. (FG3A 2202-2213)

This patient had also gone on to apply pacing to exercise which meant she was able to continue walking her dog and do some very gentle exercise at her local gym. *‘If I pace meself I find that is better for me with the exercise.’ (PP10 FG3A 2226)*

However, although pacing was a relatively easy concept to grasp, some people said they would need support to apply the principles to their own lives. Solely being aware of the concept of pacing was not always enough to being able to implement the strategies. Other factors also could influence the practical application of strategies such as pacing. A patient who was involved with several committees found that if she was chairing a meeting, she

was better able to control it, and instigate breaks. However, if someone else was in charge, this could become more difficult as:

PP2 *'There's an awful lot of people who just want to get on and they just don't want the breaks. ... You feel you're being pushed all the time'. (FG1B PP2 1753-1754)*

Outside influences, particularly in work or more formal situations could make it difficult to apply the principles of pacing activity or planning rest breaks, especially if other people were involved in the activity.

Exercise was a strategy used by other patients to help actively manage their fatigue. One participant explained how he found exercise to be beneficial, but his ability to carry it out depended on how much energy he had at the time. He also thought that if people with PSS were advised by professionals to try and manage their PSS fatigue, then the advice should be appropriate and specific for the individual. Another patient who had previously been advised by a health care professional to do some very gentle exercise had followed through on this advice. She had taken up Qi Gong, which is similar to Tai Chi, and found it to be beneficial; *'I try to do it ... every morning. And that helps me start the day'* (FG1B 1077-1082).

6.2.1.2 Strategies used to manage sleep disturbances

One participant had now resigned himself to having poor sleep for the rest of his life. *'It's just something you live with; you can't do anything else'* (PP1 FG1A 50). However, other people had implemented their own range of strategies to try and improve their sleep.

Daytime naps were one such strategy that some people drew on to help them manage symptoms of both their daytime sleepiness and fatigue.

PP5 *I, I get to a point where I've now just got to switch off for a little while. ... And it might not be sleep, it might just be sitting quickly, resting my eyelids but then I, I can have another go.*

Kate *Mhm.*

PP7 *A powernap.*

PP3 *Just creeps up on you, yes.*

PP7 *A powernap.*

PP5 *Yeah. Yes it is, yeah. (FG1B 733-755)*

Daytime napping offered some refreshment which participants were not able to experience from a night-time sleep. However not everyone was able to sleep during the day despite a poor night's sleep. One lady believed that if she were able to have a nap, she would feel better, but despite trying, she was unable to sleep at all during the day. Consequently, she constantly felt more fatigued.

Some participants had sought help from their GP who had subsequently offered to prescribe them sleeping pills. However, none had opted to use them. One reason given by one was that she thought hypnotic medication may be addictive and she did not want to become reliant on such a drug. Another said her reason for refusing it was *'I want control of me, not drugs'* (PP2 FG1A 1114).

Alternative medicines, including Chinese herbs, Shiatsu and acupuncture had been used by some people. One participant regularly had acupuncture for her pain and described her night's sleep following an acupuncture session; *'I sleep like a baby. It's a wonderful, wonderful deep restorative sleep, and I can go all the way through'* (PP6 FG1A 139-141). This phenomenon was not unique to acupuncture as someone else also described experiencing restorative sleep the night following a Shiatsu treatment.

Relaxation or meditation techniques to help sleep were an avenue which had been explored by some people. One patient told the group how she regularly enjoyed using meditations to help her relax at bedtime. She had sourced the tracks on the internet and downloaded them onto her iPad. However, despite noticing some relaxation benefits from listening to them, she did not always find that she could get off to sleep whilst listening to them. Another patient found that relaxation helped her to *'calm down and take [her] mind off ... worrying things or churning thoughts'* (PP4 FG1A 1649-1653). Therefore, although these techniques

did not necessarily induce sleep, they did seem to help distract from anxieties and promote a sense of well-being.

One patient described how he struggled with thoughts going through his mind while he was trying to sleep:

PP5 *When I'm lying awake, and my mind's churning over goodness knows what, and I can't get back to sleep, the only thing that actually gets me back to sleep was putting my TV on because that occupies my mind. And I fall asleep to the TV. (FG1A 1389-1392)*

Another patient used the radio as a similar distraction technique in order to fall asleep.

Discomfort interfered with sleep and patients addressed this in a variety of ways, depending on the source of the discomfort. One person had been able to alleviate the discomfort she experienced in her legs by propping up the end of her mattress in the hope that she would sleep better. Feeling cold at night in bed, particularly experiencing cold legs meant, perhaps unsurprisingly, that some people took a great deal of care ensuring that their sleep environment was warm and stayed warm, using electric blankets, hot water bottles, and extra blankets. However, these strategies could also affect a bed partner. One patient's wife described how her husband's use of hot water bottles in the bed was '*a bone of contention*' (AHM1 FG1A 896) as she liked to remain cool in bed.

6.2.1.3 Strategies used by participants to manage pain and discomfort

Patients used a variety of strategies to help manage their pain and discomfort. One such strategy was to push through the pain, to '*push it to the back of your mind*' (FG3A PP10 2307) and focus on something else, because '*if you concentrate on the pain it seems to get worse*' (FG3A PP10 2303). Music was an example of a welcome distraction. If it were possible to redirect attention onto something enjoyable, such as music it meant that pain would seem to reduce. However, if they also had difficulties with tolerating noise, music might not be the most appropriate distraction. Using other activities, which required physical or mental effort as a distraction from pain and discomfort, could also be more difficult to achieve during an exacerbation of fatigue.

Patients had sought help from their GPs for their pain and had encountered a range of responses. They described that, after finding a doctor who was sympathetic to their needs, they would prefer to go back and see the same doctor rather than risk receiving a negative response from a doctor who they perceived as not having a lot of understanding about their condition or symptoms. However despite being on the receiving end of some negative attitudes from GPs, (this was discussed previously in the context of fatigue in Section 6.2.1.1) there were incidences of positive responses to patients' experience of pain. One patient had been referred for '*Exercise on Prescription*' (Ayres and Pocock, 1995) by her doctor. Another patient described how a more sympathetic GP in her practice had:

PP10 prescribed the rare codeine and paracetamols for us. She said, "Oh no, just take them when ... when it's necessary." (FG3A 1780-1786)

This patient had been empowered by her GP take control of her pain medication, and taking it when she felt it would be appropriate, which for her was '*only if it's really bad*' (FG3A PP10 205).

Transcutaneous electrical nerve stimulation (TENS) devices were used by a couple of people. One patient needed help from her husband with a device which:

AHM2 Looks like a thick pen. Erm, and you click the end and it gives you, it's like an electric shock. ... And it stimulates. You've got to click it about 25 times, I mean when [his wife (PP8)] wants clicking I end up with thumb ache because (Laughter) it takes that much clicking, but it does help at times doesn't it?

PP8 Yeah. (FG3A 1403-1422)

Another patient also found benefit from wearing a TENS machine on his back and shoulders as this helped to relieve his musculoskeletal pain.

Two patients mentioned their use of alternative therapies in the context of managing their pain. As was mentioned in the previous section (Section 6.2.1.2), one participant found acupuncture to ease her pain and consequently help her sleep better. Another patient explained that as well as helping with many of her other PSS related symptoms, Shiatsu had helped to decrease her pain.

Support from family members was considered to be particularly important when the pain was a problem. Supportive significant others could be very helpful, when pain was particularly bad. One patient's daughter often would often encourage her during a pain flare by saying:

PP10 "You'll be alright." ... Just, er, just take a few deep breaths and we'll just start again" (FG3A 2586-2590)

Having supportive friends and family, who understand the variability of PSS pain, could therefore be very useful for patients, when trying to cope with an increase of this symptom.

It can be seen that patients use a variety of strategies to manage symptoms of fatigue, sleep disturbances, pain and discomfort. Several of these strategies were also recommended during the clinician validation process. This will be discussed further in Section 6.2.2.

6.2.1.4 Generic strategies used by participants in the context of several symptoms

During the discussions, patients often found it hard to separate their symptoms and talk about one in isolation. This was because the different symptoms seemed to interact with each other. Furthermore, some strategies seemed to help with more than one symptom. For example, patients therefore often employed similar strategies to managing their pain and discomfort as to those they used for managing their fatigue, in part due to these symptoms often occurring together. Pacing was one such strategy used for both symptoms, which meant that pre-planned activities could happen without a severe exacerbation of symptom, or 'crash'.

Pre-planning pleasurable activities was considered as being an important strategy for general well-being, despite the presence of symptoms as one lady explained:

PP7 Something that you anticipate that's a pleasure.

PP3 Mhm, mhm.

PP7 Which I'm sure is, is right.

PP3 Mhm.

PP9 *I think that's very major actually. ... In my ten tips I wrote ... [I say] try and have something to look forward to either daily or weekly. I think you really can. (FG3A 2250-2266)*

This lady (PP9) explained to the group how she had previously written a list of helpful tips to help other people with PSS and this recommendation was in her list.

Planned exercise was something that one patient found particularly helpful for her fatigue, pain and mood:

PP10 *Well I do a regular exercise and I've been doing it for three years. ... And, erm, I've always found it good because it, otherwise I, if I just sat there I wouldn't get up in the morning and do anything. (FG3A 2175-2180)*

Another patient who was taking part in an 'Exercise on Prescription' scheme for her pain (see Section 6.2.1.3) explained that this scheme provided her with '*a free membership to, er, [a local] leisure centre*' (PP7 FG3A 2101). Subsequently, she had been using the gym under the guidance of an instructor and having swimming lessons. As well as helping her pain, the regular exercise had resulted in the added benefit of improving both her fatigue and her mood. She described feeling more confident and positive which she attributed to taking this step in supporting her own health. However, a couple of patients had experienced a '*detrimental effect*' (PP1 FG1B 1060) from carrying out exercise:

PP5 *It's like also if you try and do some sort of exercise, even if it's just, you know, 30 minute walk a day, the, the, the repercussions sometimes ... is worse than actually doing it. (FG1B 1050-1056)*

Symptoms could be exacerbated by doing too much exercise and it was difficult for people to gauge how much the right amount was.

We have seen that having supportive people around can be helpful and conversely we saw previously (in Section 5.2.1) that having unsupportive family or friends who did not seem to understand the symptoms of fatigue and pain could be unhelpful. One focus group participant explained that she had found a source of support through social media. She

regularly used the social network internet resource Health Unlocked (Health Unlocked, 2016) and discovered:

PP7 It's just somewhere you can just vent your spleen a bit and you get information, you get ideas.

AHM2 You get support.

PP6 Yes- and you get bits, it fills in the blanks where the medical practitioners, maybe, leave off. (FG3B 2005-2011)

Although this patient did not receive much understanding from her immediate family members, she had found support amongst strangers on the internet who mutually shared their lived experiences of living with chronic symptoms.

6.2.2 Responses of participants to strategies proposed by clinicians to manage their symptoms

For each of the symptoms, various potential intervention components, which related to the particular symptom were described to participants as outlined in Table 6-1. Overall, participants responded positively to these suggested strategies. Details of their responses are provided for fatigue, sleep disturbances and pain and discomfort.

6.2.2.1 Fatigue

Several patients had already tried, or continued to use, some of the fatigue management strategies including pacing and exercise. This in itself demonstrates that patients were generally accepting of such interventions. Several patients understood the theory behind pacing but explained that it could be '*difficult to apply*' (PP6 FG1B 1023) however '*it's worth pursuing*' (PP6 FG1B 1027) because they could see the benefits. Providing the information wasn't always enough for people to be able to actually practise this skill and some people felt they would require further support to implement information that was provided in written form. Others felt confident that as long as they had the information at hand, they would be able to apply the principles. Different patients therefore require different levels of support.

Earlier, (see Section 6.2.1.1) we saw that one patient used a diary to help her map her symptoms. Within the context of planning and pacing, activity diaries were also discussed as a potential component of a fatigue intervention. Diaries were seen as an acceptable and potentially useful intervention component to help patients self-monitor their fatigue.

Exercise was again an acceptable intervention, but some people found it difficult to know where to start and how to pace it appropriately (see also Section 6.2.1). Therefore, appropriate individualised guidance is needed.

CBT was an intervention which had previously been recommended to some focus group participants as previously seen in Section 6.2.1. Further aspects of CBT interventions were also discussed as a future possible intervention for fatigue. I asked participants whether it might be useful to examine some of the thoughts which are likely to drive unhelpful behaviours. This was something which resonated with one patient in particular:

PP5 I've always been a workaholic so I have a problem that I'll, I've got something to do so I go at it and I've got to finish it. ... But the result of forcing myself to finish it is that I've got nothing left in the tank. (FG1B 1303-1314)

Spending time to examine the beliefs behind unhelpful behaviours or habits was seen as both acceptable and appropriate by all, including those who believed they were less driven by their premorbid standards. However, all participants could relate to these 'all or nothing' (Vincent FG1B 1325) behaviours and believed CBT would be an acceptable and helpful intervention which would provide patients with opportunities to examine unhelpful thoughts and behaviours.

Within a CBT intervention, it was also seen as important to have the opportunity to consider the reactions of others in society towards their disease and symptoms, particularly when these were negative. It was also felt that some PSS patients might need support to function and manage their symptoms, particularly fatigue, in social and work situations. It would therefore be advantageous to have the opportunity to explore these scenarios during a future fatigue intervention.

Participants remarked on how an inability to participate fully in every-day activities due to their fatigue, impacted on their mood. Having specific goals to enable them to participate

more fully in activities was seen to be helpful, in both managing the fatigue and improving mood. A patient's husband gave an example where his wife's fatigue was affecting her mood due to the fact her activity and participation had reduced so much:

*AHM2 And I had to really nag you to come with me just to take him
[grandchildren's dog] for a walk didn't I? But it did help you, I
think, when you got out.*

PP8 Yeah (FG3A 2546 – 2548).

Having support to set and implement specific goals, could therefore seem difficult when it came to implementing them, but the effort required could be really beneficial. Setting personalised goals was therefore seen as an acceptable component of a fatigue management intervention.

6.2.2.2 Sleep

Many of the poor sleep experiences described by patient participants were not unique to PSS, but, as discussed in the previous chapter, (Section 5.3) share similarities with other conditions. Several components from a cognitive behavioural therapy for insomnia (CBT-I) intervention, (see Table 6-1) were described to participants in order to appreciate how well they might be received as a potential intervention to improve their sleep. Although only some components of a CBT-I intervention were discussed, including some stimulus control elements (Bootzin *et al.*, 1991), due to the time constraints, this was deemed enough to introduce the concept of CBT-I treatment. The stimulus control elements which were discussed included only using the bed for sleep and sex (hence removing other activities such as crafts and computers from the bedroom), getting up if not asleep after 15 minutes, anchoring the wake up time and avoiding day-time napping (Bootzin *et al.*, 1991).

A discussion around sleep hygiene and CBT-I components followed. Some participants had already tried some components and one lady had previously received one-to-one CBT-I over several weeks.

Sleep diaries are used in CBT-I to measure outcomes and monitor sleep efficiency (the percentage of time spent in bed being asleep). Some patient participants had previously

been asked to complete sleep diaries at their clinic appointments. Although the purpose of collecting the sleep diary data at the clinic was primarily to measure sleep outcomes and plan treatment, it had surprising benefits:

PP6 That sleep diary, er, that I've done for [clinic] - that was incredible. That really made me think, 'cause ... we're trying to find answers about patterns and all this. ... And I think all of a sudden when you start to ... log your sleep and ... you focus on it ... it sort of raised lots of things that I thought, "Ah, maybe there are some things I could do...". I found that sleep diary very, very useful.
(FG1A 654-665)

This patient found that by documenting her sleep for a couple of weeks, she formed an awareness that her sleep problems were actually part of her disease. The process of completing the diary also helped prepare her to make changes after seeing patterns emerge in her sleep diary. She subsequently felt ready to implement any suggested behavioural changes to try and improve her sleep.

Another technique proposed to the group was to remove clutter and activities from the bedroom including books, work, mobile phones, televisions, crafts etc. The participant who had undertaken CBT-I had already been advised to do this as part of her therapy and had subsequently carried out this advice and continued to implement it after she had completed her therapy. Another participant who was hearing this advice for the first time during the focus group started to make immediate plans to practically change her bedroom environment when she returned home:

PP6 It's made me look at our bedroom, which is basically like a warehouse 'cause we're putting a Velux window in and...our bed is ancient, it's 15 years old and it desperately needs changing. ... I even thought about those just practical things like maybe, "Yes, we need to get the bedroom more comfortable." So things like taking out those, you know - gadgets and things ... you're doing as much as you can - practical things. (FG1A 1591-1611)

For this patient, completing the sleep diary and having access to this information was enough for her to make changes to her bedroom environment.

Although other participants had not formally had CBT-I, a few participants recognised some of the components discussed as they had previously tried to implement them themselves. Anchoring the time that someone would wake up in the morning was one such strategy that had been put into practice by one participant who gets up at the same time daily for her work. This is where the wake up time is set the same every morning e.g. 7am and means rising at this time every day, including weekends, regardless of how well the person had slept the previous night. Other people also indicated that they would be willing to try it if it was part of an intervention which aimed to improve their sleep. However, one participant had a different reaction. He said he would *'find it difficult fixing a time because it depends on the sort of night [he'd] had'* (PP5 FG1A 1447-1448). He explained;

PP5 *if you do eventually get to sleep what's the point of deliberately waking yourself up? You're having some sleep, thank God. Let me, let me keep it.*
(FG1A 1676-1678)

As shown in the previous chapter, sleep is regarded as a finite resource which on first thoughts he did not want to squander, even as part of an intervention to help him in the longer term. He seemed resistant. However, after being given the rationale behind some of the intervention components being mentioned he agreed that he could see the reasoning behind it, but if he were to try these techniques he would have *'to see some, erm, success'* (PP5 FG1A 1844-1845) after implementing any such strategies in order to continue with the treatment.

With regards to sleep onset difficulties, a technique which is recommended to patients is that they get up after 15 to 20 minutes if they have not fallen asleep. Participants generally said they would see this advice as being acceptable. Two people already did this, one of whom had received the CBT-I intervention previously. However, one person who regularly implemented this advice and gets up to read in a chair if she is unable to get to sleep, encounters a problem:

PP2 *Next thing I know it's two hours, three hours later. ... I haven't gone back to bed. I'm just sitting in the chair. ... And I've just fallen asleep.*

Kate *Oh, you've fallen asleep in the chair?*

Despite intending to return to bed when she feels sleepy, she regularly finds that she has fallen asleep in the chair. There were also others in the group who disagreed with this idea and said that they would prefer to stay in bed as in their experience, they would eventually doze off.

Another technique; sleep restriction (Spielman *et al.*, 1987) was proposed to the group. In this technique, the average amount of sleep someone has each night over week is calculated. Thirty minutes is added to their average sleep time and this is the amount of time that they are permitted to be in bed. The exception to this is if someone is experiencing on average less than 4.5 hours sleep per night meaning the minimum amount of time a person would ever be restricted to is 5 hours, even if they were getting on average a lot less than this per night ordinarily. This suggestion received a mixed response from participants. It initially seemed counterintuitive to the group; *'The thing is, if, if you're not sleeping what's the point in not going to bed?'* (PP1 FG1A 1671). For this reason participants felt that again, they needed a good rationale as to why this might be advised. They understood the rationale which was to be able to regulate their sleep and for them to begin to associate being in bed with being asleep, not awake. After being presented with a good rationale, they acknowledged that *'the patient too has to be willing to experiment'* (PP4, FG1A 1830). Most participants in theory would be willing to try these techniques if they thought that their sleep would improve as a result of the changes that they had made and if they were able to see some improvements relatively quickly after applying these techniques.

6.2.2.3 Pain

The discussion which took place around pain management strategies, included components of activity management, CBT (Ehde *et al.*, 2014) and acceptance and commitment therapy (ACT).

As with the other symptoms of fatigue and sleep, patients viewed symptom diaries as being an acceptable and potentially useful tool for managing their pain symptoms.

The focus of ACT helps the patient accept their pain, to refocus their attention towards opportunities in the present and to realise valued goals (the commitment) (McCracken and Vowles, 2014; Veehof *et al.*, 2016). Strategies including meditation, exercise and balancing activities and rest were not covered in great detail, as they had been discussed as part of a fatigue strategy management plan (Section 6.2.2) or had previously been raised by participants as being useful coping strategies which they already use.

Following a description of ACT, one lady described how accepting her breast cancer diagnosis several years previously had helped her while she was undergoing treatment. She said in the early stages following her diagnosis;

PP6 *I reeled and reeled and reeled against the disease because I was ... getting worse and worse and worse. (FG3A 2416-2417)*

However, following a conversation with someone who had encouraged her to try and accept her diagnosis and stop fighting, she came to the realisation that if she could accept it, she would expend less energy and redirect her energies to getting through the next stages of her treatment. Furthermore, she was able to apply this acceptance to her PSS diagnosis and the pain and discomfort that came along with it. Through accepting her disease and its associated symptoms, she felt better in herself. Another participant shared this view:

PP6 *If you could, if you could ... train your brain to accepting of the disease ... life would be so much easier I think. ... It really would. ... Acceptance is the key word' (FG3A 2469-2489).*

The commitment aspect of ACT echoed with some of the strategies patients already used (see Section 6.2.1.3). It could mean choosing to do a valued activity, rather than avoiding it. Avoidance can take place to prevent experiencing further unwanted symptoms. One focus group member could see how it would be easy to avoid activities which seem to heighten her pain. She explained that her back pain is aggravated whenever she attempts to move logs in her log pile. However she had made the choice to continue with the activity and found '*eventually it [the pain] goes away*' (PP7 FG 3A 2401). Patients found that if they allowed their pain to receive their full attention, rather than a task at hand, it meant that they were less likely to complete the activity and that their pain would be more intense.

- PP10 *I think if you think more of the pain it, the pain's worse.*
- PP6 *It, it gets on top of yous.*
- PP10 *It gets on top of you, yes.*
- PP8 *Mind over matter.*
- PP7 *It is- You just learn to, kind of, shove it.*
- PP8 *I think if you've got a job to do as well, you've got to get it done.*
- PP5 *Well if you've got something to do.*
- PP8 *Yeah, you have to get it done (FG3A 2329-2354).*

CBT, meditation and ACT were all interventions that patients would welcome, if offered, as part of a plan to help them reduce manage their symptoms. Furthermore, some patients already used several of the strategies themselves, therefore had 'bought into them' but they would value specific and appropriate support to better self-manage.

6.3 Discussion

Participants had experience of a range of interventions, and were mostly willing to try out new ones, particularly if they were individualised and time was taken to explain the rationale behind them.

Starting an activity and seeing it through to completion was a self-management strategy which several patients had adopted. In a self-management book written for people with CFS, the author describes people who push through activities to completion without stopping for rest as being 'starter finishers' and how this behaviour can be self-defeating (Pemberton, 2009). Pushing through the fatigue was seen as a way of fighting the symptom by some participants, despite repeatedly experiencing negative consequences from implementing this strategy. Conversely, in the context of pain this strategy was seen as

potentially being helpful. Patients reported how committing to a task and seeing it through to the end could help distract from their pain. However, committing to an activity did not mean that it cannot be broken up and interspersed with rests. Several patients had reaped the value from pacing their activities by breaking down them into smaller chunks and taking regular rests. This strategy is used within in both fatigue and pain management interventions (Hewlett *et al.*, 2011; Hewlett *et al.*, 2015; Andrews and Deen, 2016). However, pacing was a skill which could be difficult to apply, in part due to self-defeating behaviours. Therefore investigating these self-sabotage behaviours (Hewlett *et al.*, 2015) may be a helpful component of an intervention to manage pain or fatigue.

In addition to using pacing strategies, some patients had already used diaries to self-monitor their symptoms, found them to be useful and regarded them as an acceptable intervention component which patients could use to observe patterns in their own behaviours. Diaries are a tool which used within symptom management interventions for fatigue (Hewlett *et al.*, 2011; Hewlett *et al.*, 2015) and insomnia (Mairs and Mullan, 2015) and could be used in a future PSS symptom management intervention.

Some patients used exercise to help with their fatigue, pain and general well-being. Exercise is recommended in the management of PSS fatigue (Price *et al.*, 2016). This qualitative work begins to show that patients need support to tailor their exercise and to start at a level which is appropriate for them. Some patients were able to work this out for themselves, while others require more individualised support and guidance.

It can therefore be seen that patients require different levels of support. In this study, some patients recognised that making some specific changes to their behaviours helped them to better manage their symptoms. They were able to implement these behaviour changes if they had access to the information which explained what to do. However, information itself was not enough for others to feel that they would then be able to independently make lifestyle changes and they require more support than purely information alone. One study (which included PSS patients) found that written self-management information for fatigue may have more impact with supporting patients to manage their own fatigue if the information is handed to the patient directly by a healthcare professional and they are given a follow-up appointment to discuss the written advice. This extra support may provide more opportunities for behaviour change to occur, in the context of fatigue management (Hart *et*

al., 2016). The following chapter (Chapter 7) discusses different levels of support in more detail.

This study has begun to show the importance of providing patients with a rationale for interventions where they are able to see improvements in their symptoms or functioning as a result of carrying out an intervention. Conducting a 'behavioural experiment', where a new behaviour is tested for a trial period may be a useful intervention component. There is some evidence that this strategy is beneficial in anxiety disorders (McMillan and Lee, 2010) and may be particularly useful if a patient is anxious about changing a behaviour or sceptical about its potential for benefit.

This study has provided some evidence that once a self-management skill is learnt for one symptom, patients are able to apply the same strategy to other symptoms. This is important, because if a patient has several symptoms, it may not matter which is addressed first in a symptom management program, as the technique may have a carry-over effect and help them with managing other symptoms, improving their autonomy in managing their own disease. This concept could also be considered as patient activation, which is '*an individual's knowledge, skill, and confidence for managing their health and health care*' and can be measured with the Patient Activation Measure (Hibbard *et al.*, 2005).

This qualitative study has provided direction on which specific strategies and intervention approaches could help with symptom management in PSS. For example, when patients hid their fatigue from those around them, it often resulted in increased expectations from others. A cognitive behavioural approach could therefore be used to challenge unhelpful beliefs around fatigue and equip patients with the skills required to describe or explain their disease and its symptoms (including fatigue) to others, when appropriate (Rimes and Chalder, 2005; Hewlett *et al.*, 2011; Dures *et al.*, 2012; Knoop *et al.*, 2012).

Patients reported that sometimes support for their fatigue symptoms from other people could be enabling. Conversely, sometimes seeking support from others was regarded as being disabling. Context and individual beliefs therefore determined when support from another person with fatigue symptoms might result in either increased independence, or greater dependence. A tailored level of support with acquiring this skill may therefore be appropriate.

Exercise, particularly exercise which was paced or gentle, was also used by patients to manage their fatigue. This is in line with evidence in the literature for physical activity interventions for fatigue in fibromyalgia (Macfarlane *et al.*, 2016), RA (Cramp *et al.*, 2013) and CFS (White *et al.*, 2011) as well as evidence from a small study of aerobic exercise in PSS (Strombeck *et al.*, 2007).

Some patients had naps during the daytime to manage their daytime sleepiness. However daytime naps, particularly when taken during the afternoon, are associated with reduced cognitive functioning in CFS (Gotts *et al.*, 2015) and are generally discouraged as part of a CBT-I intervention (Perlis *et al.*, 2005). Therefore, daytime naps are not necessarily an appropriate coping strategy.

One patient who had completed a course of CBT-I, continued to carry out the techniques including stimulus control, yet still continued to have poor sleep. CBT-I will not provide an effective solution to everyone with PSS-related insomnia.

Patients accessed support from others, including their family members and internet support groups in order to help them cope with their pain and discomfort. Group support, provided either online or through face-to-face group interventions or patient support groups, may also be beneficial. Interventions which include an element of peer support have shown positive results on a range of outcomes in patients with a range of conditions who experience chronic fatigue, insomnia and chronic pain (Hewlett *et al.*, 2011; Thomas *et al.*, 2014; Matthias *et al.*, 2015; Kothari *et al.*, 2016).

Influence of others can prevent people from pacing. Assertiveness training is a skill which might be beneficial to some people. This has been recognised by others who have developed and tested fatigue and pain interventions. Assertiveness training is incorporated into CBT fatigue management for RA (Hewlett *et al.*, 2015) and communication skills form a module of an online self-management tool for fibromyalgia (Sparks *et al.*, 2016).

Patients found it useful to monitor their symptoms using symptom diary. Self-monitoring is a behaviour change technique which has been used in interventions to promote physical activity in RA (Larkin *et al.*, 2015), is likely to be acceptable to PSS patients and could be used as a component of a symptom self-management intervention.

This study has begun to show that partner involvement in future symptom-management interventions could improve understanding and therefore support. Previous research has found differences between how couples relate to each other in the context of one partner having RA and couples were categorised into one of three groups: 1) '*The shared illness management*' group, where both partners would attend appointments and make decisions together about how to manage the condition, 2) '*The ill partner in charge*' group, where the person with RA made autonomous decisions about their own disease management and 3) '*The conflict over management*' group. In the third group, there was conflict in the relationship as the partner was dissatisfied about how the person with RA was managing their condition (Mann and Dieppe, 2006). Providing opportunities for partner involvement and supporting patients to communicate their needs effectively and assertively may therefore mean less conflict and result in the person with PSS feeling more understood and supported by their family. Further research would be required to investigate illness-related interaction in couples and families with PSS, but it is possible that those who have understanding partners (in the context of how they manage their PSS fatigue) experience less conflict than those whose partners did not support the way they managed their PSS symptoms. However, relatives should be included in face-to-face interventions and literature could also be made available for friends, relatives and employers which gives further information about the disease and symptoms. Increased awareness amongst friends and family may result in increased support and ultimately have a positive effect on mood.

The way a person with PSS perceives their support from friends, family and health care professionals may have an impact on their mental health. A recent study has demonstrated that PSS patients who had either functional or self-reliant psychological profiles had lower fatigue scores than those who had dysfunctional or alexithymic (alexithymia is difficulty differentiating emotions) psychological profiles (van Leeuwen *et al.*, 2015). The self-reliant group did not generally have good social support but they did not demonstrate negative thinking styles or display avoidant behaviour and were able to both describe and identify their feelings. Perhaps the perception of poor social support becomes a self-fulfilling prophecy. Addressing both negative thinking styles and avoidant behaviours within a CBT intervention could benefit patients with PSS and ultimately impact on their fatigue levels. Equipping patients with assertiveness skills and helping them with being able to

communicate with others about their fatigue could also be beneficial and making literature available to patients to pass on to others could help increase self-efficacy. Educating healthcare professionals about the impact of PSS should also be considered. Support from a healthcare professional was also seen as being really important. '*Believe my symptoms*' was a priority statement in a concept mapping study identifying the needs of patients (including some with PSS) attending a generic fatigue clinic (Hackett *et al.*, 2016b). It is essential that symptoms are believed and acknowledged by HCPs during appointments and that they are not easily written off, for example as a symptom of old age as this can be devastating to patients.

6.4 Summary

In this chapter, I have summarised the strategies patients used to manage the symptoms of fatigue, sleep disturbances and pain as well as the response of patients and partners on potential future self-management intervention components. In the next chapter, I summarise potential modes of delivering future intervention components.

Chapter 7. A future model of care

7.1 Introduction

This chapter reports further findings from the focus groups and discusses a model in which intervention might be delivered to manage fatigue, sleep disturbances and pain for PSS patients. In this study a partially formed intervention model was presented to patients due in part to iterative process of the focus groups. It had already been suggested by participants that different patients require different levels of support (see Section 6.2.2). A model offering different levels or steps of care, with increasing intensity has a theoretical basis having already been developed and applied in other areas such as in chronic pain (von Korff, 1999) and in mental health (Bower and Gilbody, 2005). In order to shape an intervention model further, it is essential engage in a dialogue with stakeholders as this will give an indication as to whether such a model is likely to be implementable (Craig *et al.*, 2006).

7.2 Aim

To determine how a future intervention package might be delivered within an NHS setting

7.3 Method

The methods used for data collection and analysis are the same as reported in Section 5.1. Participants were asked at the end of each focus group discussion topic about possible modes of delivering the intervention components for each of the symptoms of fatigue, sleep disturbances and pain. There was also dedicated time to discuss modes of delivering future intervention components for all three symptoms, specifically allocated at the end of the third focus group. Participants were asked how this might look in an overall structure for a future model of care.

The rough model presented to participants incorporated a low intensity Level 1 intervention (such as written information and access to local peer support) which would be available to PSS patients in addition to their 'usual care'. The consequence of such an approach would mean that at diagnosis, everyone would be offered Level 1 care. This first step intervention

might include with written information about the condition as well as information on local support groups and appropriate websites and the option to attend a group session for recently diagnosed patients.

It was proposed that a Level 2 intervention might be specific computerised or face-to-face group therapies targeting the specific symptoms of sleep, fatigue, pain and discomfort. Over time, according to patient needs, the range of therapies could be expanded to include other specific symptoms which are important to patients and impact on their lives, such as anxiety and worry, low mood and dryness.

It was suggested that a Level 3 intervention could be individualised therapies for these symptoms, to be made available to those who require one-to-one, face-to-face interventions. All levels of intervention could be available within rheumatology services or some components be made available via other specialist services such as pain management teams.

Participants were asked to contribute their opinions and ideas about these ideas, to suggest any additional ideas or to add further to this proposed model further that they would consider as being particularly helpful.

7.4 Delivering symptom management interventions

In the first instance, patient participants expressed a need for personalised care, where they were able to make an informed choice about their care. The main reason for a menu of options was that symptoms manifest themselves differently in different people. They are *'like a bag of liquorice all sorts. ... Everybody's got different flavours.'* (PP5 FG3A 1192-1198).

AHM2 This is the trouble because for some fatigue's the worst problem and some it's, er, depression that's the worst problem.

PP8 There's no two alike are there? (FG3B 424-427)

Patients did not want their treatment pathway to be decided solely by clinicians. Instead, this was something they wanted active control over, providing the treatment or support they required was available. One participant described that he would like *'a list, a menu for*

the whole thing but then in, in each subsection a menu' (PP5 FG3B 787-788). Another noted that they wanted *'a support mechanism in place ... that enabled [them] to decide what [they] needed'* (PP7 FG2B 945-946). Patients wanted to have a conversation with a health care professional about the available options in order to make an informed choice about their care. There was a perception that choice and availability of different therapies and options *'would go a huge way towards helping with moods and the confidence.'* (PP5 FG3A 950-951). Thus, providing options where the patient could access what they perceived would be helpful for their individual circumstances, would be empowering.

The possible modes of delivering interventions for the range of symptoms were discussed. Following patient feedback in Chapter 6 (Section 6.2.1.1), it was suggested that differing levels of support would be needed for different patients.

7.4.1 Level 1 – Information provision and access to peer support

In the first instance, the participants stressed the importance of having access to general information about the condition at diagnosis. The information is not only important for the person with the diagnosis, but can also empower the patient to educate others about their disease, including health care professionals, friends, family and colleagues. However, there was a major drawback, to receiving information verbally at diagnosis.

PP7 *'Cause I think when you're diagnosed the words you hear are, "Incurable, but we can treat, but the treatment's iffy."*

PP8 *That's right.*

PP3 *Yes.*

PP7 *That's all you hear, you don't hear anything else. (FG3B 1628-1635)*

Patients felt limited as to how much information they were able to absorb at this time, as they were processing the fact that they have a systemic, incurable disease. They stressed the importance of also being provided with written information about their condition, including information on benefits and contact details of patient organisations and web addresses for further information which they could access as and when issues arose. Having

accessible written information was also empowering, as it can be given to others and used as a tool to help explain about the disease and how it can affect people with PSS.

Furthermore, participants believed it would be beneficial for them to access others with the same diagnosis for some kind of support and this would be an opportunity to acquire further basic knowledge or '*guidance*' (PP9 FG3B 1849) about their disease. One lady described her desperation to meet other people with PSS 30 years previously when she could think of no other way of meeting others who shared the same diagnosis.

PP9 I agreed to one or two tests that I shouldn't have agreed to really, just to see what other people [with PSS] looked like. (FG3B 1667-1668)

Most participants thought that a group offering information on their disease, some basic self-management advice and the opportunity to meet others with PSS should be available several months after being told they had PSS, which would give them space to process their diagnosis. They thought newly diagnosed patients may have more questions and opportunities for further exploration of these ideas in a facilitated group could be more useful at this point. However, one patient had a differing view about the timeframe that this should be available '*I think I'd want to know straight away*' (PP7, FG3B 1827-1828) and she said she would have been keen to have the information about such a group from her consultant at the time of diagnosis.

In the implementation of such education groups, participants thought that it is critical to provide enough information, whilst at the same time giving patients space to consider any new information about their condition and to decide how they wish to manage it. This is a fine balance as participants felt that they did not want to be frightened by being provided with too much detail about possible future outcomes.

PP7 You've got to give them that space to understand what's going on themselves and realise how they might want to manage it. So really it's the support to them to learn how to manage it rather than to tell them what might or might not happen in any great detail. (FG3B 1892-1895)

Participants proposed that a second follow-up group at this point, would provide an opportunity to ask further questions about the condition as well as providing a further

opportunity to meet others who were sharing the experience of coming to terms with their diagnosis.

People taking part in the focus groups thought that the advantage of having access to groups with facilitated discussion by a knowledgeable health care professional could help them process their own thoughts about the disease through the discussion process and reflection between group sessions. This finding implies that a purely didactic approach may not be appropriate.

PP7 Because you can be asked a question and you can either answer with thought or spontaneously but as the conversation goes on, that question in your mind is still churning away and so eventually you are going to get to the root, perhaps, of what the problem is, or something you'd never thought about. ... So you're going to get a far more, erm, satisfying... Response to yourself, as it were, if that makes sense. (FG2B 1827-1838)

Some participants explained that they would also have valued meeting an “expert patient” soon after diagnosis. This would be a patient who had been diagnosed for longer and was willing to share their experiences. One patient described how he had once been admitted to hospital for major surgery and had experienced meeting an expert patient;

PP5 And someone else who had gone through that before me was a volunteer to come into the hospital when I was in there and sit with me and talk to me about their experience and their, their life post-bowel surgery. Erm, now whether there is a transference between that sort of approach and Sjögren's, I don't know. (FG2B 1657-1660)

The participants liked the idea of having access to a patient who, with more experience, had already walked a similar path to them ‘As long as they are, they are able to be reasonably positive about it’ (PP5, FG2B 1668). They thought it could ‘depress you’ (AHM2, FG2B 1672) if the person attending the focus group had relatively mild symptoms but the experienced patient had many kinds of problems associated with their disease, as they might think ‘this is what's going to happen to you.’ (PP1, FG2B 1675).

It was therefore important to carefully select a patient who had been diagnosed for some time, to be certain that they would strike the right balance of sharing experiences but not overburden newly diagnosed patients with frightening stories.

While the focus group participants were very much in favour of groups, they had opted to come along to the focus group in the first place and may be more at ease in group situations than others. They acknowledged that there may be some patients who after receiving a PSS diagnosis may not want to access a group. Some people may find that a written information pack provided at diagnosis including contact details of patient organisations and web addresses for further information is sufficient. They thought such a pack should contain details on where patients could access further support as and when issues arose.

Participants discussed the pros and cons of accessing support via an online forum. One patient (as discussed earlier in Section 6.2.1.4) had first-hand experience of this for one of her comorbidities, as well as a PSS specific forum and clearly found these forums a useful source of support;

PP6 The forum takes up where the medical side leaves off, or where if your family don't want to discuss it, or whatever. And we go on and we exchange lots and lots of ideas and things, we get lots of, you know, I mean everybody says, "We're not there..." Nobody's there to give medical advice. But it's just somewhere you can just vent your spleen a bit and you get information, you get ideas.

AHM2 You get support.

PP6 Ye- and you get bits, it fills in the blanks where the medical practitioners, maybe, leave off. (FG3B 1994-2004).

Therefore, although professional-based expertise and knowledge is useful, it can be supplemented by expertise and shared experiences from other patients who also live with the disease and/or symptoms.

7.4.2 Level 2 – Accessible therapy to manage specific symptoms: Computerised therapies and group symptom management support

Although having access to information about PSS, participants felt that further specific symptom management support would be required for patients at different times. As there is such heterogeneity of symptoms between patients and because a particular symptom could be more troublesome at a particular time for the same individual, it was again, important to have choice. A menu of different specific digital therapy interventions which could be accessed via a website was one such potential option that was put forward in the focus groups. There were different views about this potential mode of delivery.

There were some benefits that members of the focus groups identified regarding digital therapy interventions. One participant saw the potential of this kind of support being available to more people than face-to-face therapy might be. She also thought *‘one has to be careful about costs’* (PP4 FG1B 1998) and saw this as a cost-effective way to deliver an intervention to many people, which was also realistic to achieve.

Although the idea was new, participants generally thought that they would be willing to try this sort of intervention and *‘If it works fair enough, if it doesn’t well you can move onto something else’* (PP1, FG1A 2023-2024). One participant said she saw the attraction of a computer intervention to people who were planning and designing interventions and was positive about it herself as she liked to use computers.

A husband of a person with PSS saw further advantages with computerised interventions, as it is possible to improve and modify them; *‘when you do something on a computer it’s there and it can be improved’* (FG3B 924-925). He also thought that it would be relatively easy to refer patients for such interventions. For example, a GP could refer patients during a consultation, thereby making it immediately accessible to a person with PSS as it is required. Another participant thought that it would require less *‘manpower’* (PP9, FG3B, 821), and thereby increase accessibility.

There were also less favourable opinions regarding computerised therapies. One household member pointed out the age demographic of a sizeable proportion of those with PSS and how this could be a barrier to accessing computerised therapies.

AHM2 A lot of people with Sjögren's are, are older and a lot of people, erm, either don't want to or haven't got the knowledge for computers and stuff like that. (FG2A 1666-1667)

Another patient participant who worked with computers was willing to try such a therapy, but for him *'face-to-face is still the preference'* (PP5, FG2B 1703-1704). The reason for the reservations were

PP6 Because you don't get any feedback at all on a computer.

PP5 Yeah, because if you are telling everybody face-to-face, you can see looking at their face whether the eyes and the mouth agree. (FG2B 1710-1713)

One participant's reason was simply *'I hate computers'* (PP8, FG3B 879). Participants thought that computerised therapies would require commitment and motivation from patients. One participant considered herself as *'too lazy'* (PP9, FG2B 1869) to work through an intervention on a computer without a therapist.

One way around the potential problem of lack of commitment was that digital therapies could potentially be offered with additional face-to-face, Skype or telephone appointments to give additional support or coaching to a person who was working through a computer therapy. This was met with a favourable response, with one patient participant seeing a potential active role for himself, in supporting people through the process:

PP5 I can imagine that if – this is just me – I can imagine because of my, erm, my push to volunteer for things, if there was a digital pathway, I could see I could offer to be a digital advisor and take people through it. I'll sit in front of the computer with you.

AHM2 Yeah, you could be a digital buddy for everybody. (Laughter)

PP5 I could do that.

PP9 I'll come along with you. (FG2B 1942-1950)

Although there are some potential disadvantages of computerised therapies, there have been many advantages highlighted. This is potentially an intervention which would require less manpower than some traditional face-to-face therapies and could be made accessible to large numbers of people who needed it quickly. Refinements could be made to constantly improve it and it could be enhanced by additional support being provided by expert patients or clinicians. It could be a lower level intervention which could be made available to people who are experiencing particular difficulties, such as with sleep (e.g. CBT-I). If this intervention does not help to improve their symptoms, there is potential for a higher intensity intervention to be offered (face-to-face individual appointments).

7.4.3 Level 3 – One-to-one therapies

Participants highlighted the advantages of having face-to-face therapy. These included *'human contact'* (PP6 FG1B 1953) and the fact that it was *'more personal'* (PP1 FG1B 1961). Another participant explained the reason face-to-face suited her was *'you can connect and you can, I think you can open up and express more when you're face-to-face'* (PP3 FG1B 1963-1964).

Participants had particular expectations of face-to-face therapies. Being able to have *'faith in the other person'* (PP9 FG3B 886) and *'the attitude of the person'* (AHM2 FG3B 894) were essential prerequisites, alongside listening skills and the knowledge of the therapist. Participants are able to tell if a therapist genuinely believes what they are recommending, or if they believe what their patients are telling them.

AHM2 I mean you sat there, I mean I can read your face and, you know, I know if you're telling me something and, that you believe it, sort of thing, you know, through your eyes and your expressions. (FG3B 906-908).

I anticipated that for those having to travel long distances to access therapy, that this may be a problem. However when this was put to participants, no one saw it as a difficulty. However, again, the participants who had chosen to take part in the focus group were motivated to travel to a face-to-face meeting and this viewpoint may not be representative of the PSS population as a whole. The major disadvantage of face-to-face therapies was thought to be the resources that would be required.

One participant was very pragmatic about provision of therapies, and making them available for all who could benefit from them.

PP4 Cause I think one has to be careful about costs ... of therapies and what is available ... and not create expectations ... that would be unrealistic. ... And if you can come up with a, a lower cost recommendation that might actually be delivered... (FG1B 1998-2021).

She saw potential in rather than making a therapy that, although desirable, may only be available for a small proportion of people who might benefit, it may be better to look at alternatives which could be accessed by more people and that could be deliverable.

Having the option to have a partner or relative present during health care appointments was important for some patients. There was a perception that involving family members in any therapy would help the family member understand more about the condition and their attendance would be indicative of their support. A spouse of a patient echoed this and said she would like to be present during any face-to-face CBT her husband might have in the future, as this could help her gain further understanding of his symptoms and emotions.

7.5 Discussion of stepped model of care and PSS care pathway

An illustration of the model can be seen in Figure 7:1. There is support for managing each of the symptoms of fatigue, sleep disturbances and pain, with the intensity of the intervention increasing with each level of the model.

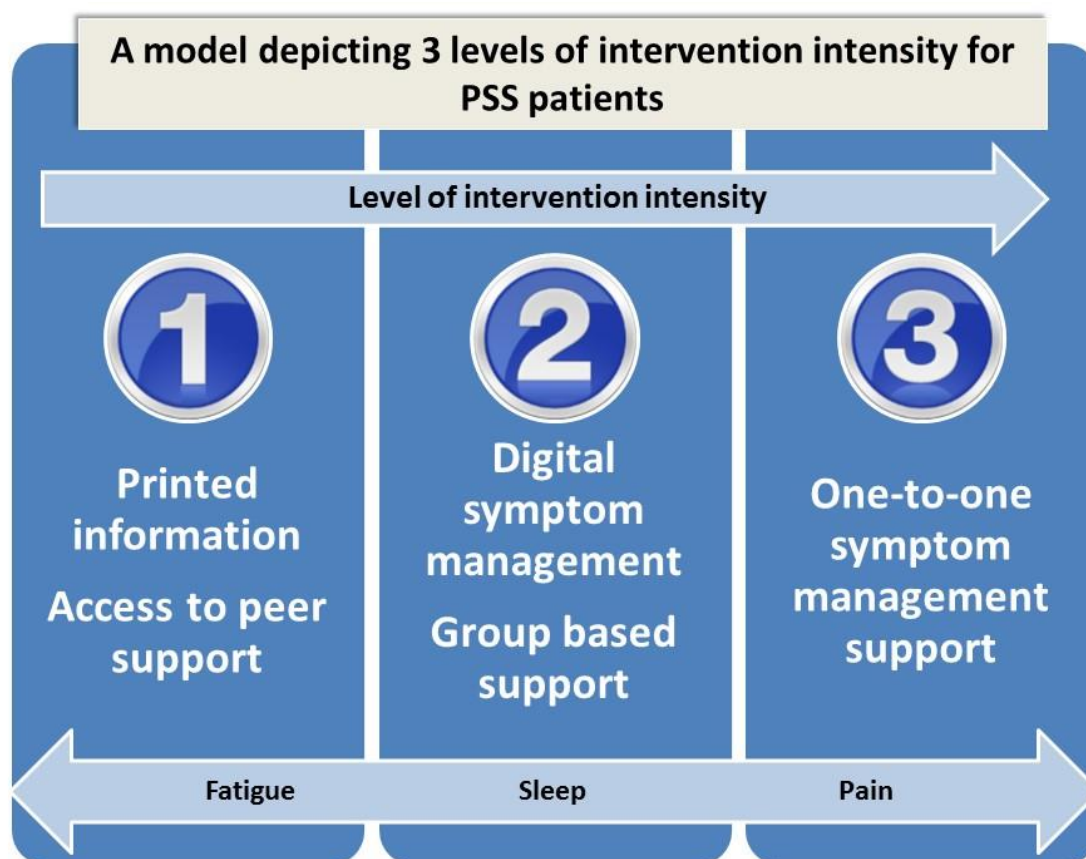


Figure 7:1 The intervention model

During the focus group discussions, patients explained that it was very difficult to absorb information at the time they received their diagnosis. The literature shows that type 2 diabetes patients also find it difficult to process the information they are given at the time they are given their diagnosis as at this time they may be experiencing a range of reactions including shock, despair and anxiety (Beeney *et al.*, 1996; Gillibrand and Flynn, 2001). However, despite potential difficulties processing information, type 2 diabetes patients still feel it is important to have detailed information at diagnosis (Peel *et al.*, 2004). In this PSS study, patients said they would also receive an invitation to one or more face-to-face group meetings where they could access further information about the PSS, to meet a patient who has lived with the diagnosis for some time, the professionals who may be involved with their care as well as meeting others who have also been recently diagnosed with the same condition. It should be noted once more however, that the patients who saw the value on this approach, had themselves opted to take part in a focus group. Within the written information which would be provided at Level 1, might also be information about information groups for people who have recently been diagnosed. Furthermore, it would

contain information explaining what is available in terms of specific symptom management support at Levels 2 and 3, and how to access it if required.

Level 2 interventions (digital therapies and groups for symptom management support) could be made available to those who were experiencing problems with specific symptoms including pain, fatigue and difficulties with sleep. This could take place with guidance initially from a trained allied health professional who would take on a coaching role. Patients in the focus groups were keen to have support from other patients and some were even keen to provide that kind of support to newly diagnosed patients themselves. Experienced patients therefore, have a potential role to play in the delivery of these interventions. This possibility of patients delivering interventions is not a new concept. Patients have a history of delivering self-management interventions to other patients in schemes such as the Expert Patient Programme in the UK NHS. This was based on the Chronic Disease Self-Management Programme which was developed in the US. This was a lay-led, training programme for long-term physical conditions which demonstrated some cost reductions, improvement in self-efficacy and health distress (Lorig *et al.*, 1999; Lorig *et al.*, 2001). The UK Expert Patient Programme also demonstrated an improvement in self-efficacy in the short term, although this programme did not result in improvements in overall quality of life or reduce access to health services (Foster *et al.*, 2007; Griffiths *et al.*, 2007; Greenhalgh, 2009). A further study by Lorig and colleagues compared a lay-led approach with a non-lay-led tailored self-management programme in arthritis patients which was delivered via the mail and 'usual care' (Lorig *et al.*, 2004). Both the lay and non-lay interventions had significant benefits over usual care and it has therefore been argued that many people do not need to access a group or a face-to-face programme to attain the capability to self-manage (Taylor and Bury, 2007).

Focus group participants stressed the importance of having choice available at Level 2. This would mean that if computer modules or groups which target specific symptoms were available, patients would have the option to choose the module(s) or group(s) that they felt would be the most helpful for them. Internet-based interventions have been criticised for having high attrition rates (Todkill and Powell, 2013). However two systematic reviews of adherence to anxiety and depression web-based CBT interventions found that attrition rates are similar to face-to-face interventions for these conditions (Christensen *et al.*, 2009; van

Ballegooijen *et al.*, 2014). If a patient chooses a digital intervention, a health care professional or trained patient might offer support at the beginning, midway and after completion of the module, as my findings show that patients think this accountability would motivate them to complete the work within the module. However, a recent trial of computer-based CBT to improve physical activity with and without additional coaching demonstrated similar improvements in both groups (Alley *et al.*, 2016). Further research is required to determine whether additional coaching is likely to increase the effectiveness or adherence to a digital intervention in this patient group.

The focus group participants had vocalised their awareness of stretched resources in the NHS and saw both digital and group symptom management as being a way of striking the balance between potential cost and reach to patients who need the support. A tailored one-to-one clinic-based intervention for PSS patients with fatigue, which incorporated behaviour change techniques (e.g. goal setting) resulted in clinically meaningful and statistically significant improvements in fatigue (Hackett *et al.*, 2016b). However, most UK PSS patients do not have access to such clinics (Hackett *et al.*, 2016b). Internet-based health communities e.g. patientslikeme® (PatientsLikeMe, 2016) can offer peer/social support but they are not designed specifically to support PSS symptom management/behaviour changes. Internet-based behaviour change interventions have shown improvements in self-management behaviours and symptoms across a range of conditions (Bantum *et al.*, 2014; Eccleston *et al.*, 2014; Hou *et al.*, 2014; Zachariae *et al.*, 2015) and therefore, such Level 2 interventions offer a potential solution to PSS patients who currently have little support to self-manage. Furthermore, such interventions would fulfil the forthcoming BSR and BHPR Guideline for PSS, which recommend that patients have access to appropriate online resources for symptom self-management (Price, 2017).

One participant expressed concerns about computer literacy in older patients with PSS. However, a recent report demonstrates that 89% of those aged 45-54 and 82% of 55-64 year olds accessed the internet daily or almost every day during 2016 (Office for National Statistics, 2016). With the average age of PSS onset being in the early 50's (Qin *et al.*, 2015), most newly diagnosed patients are likely to have internet access, and the proportion of those who do regularly access it is likely to increase. However higher levels of disability, as well as lack of skills and equipment are two of the main barriers to internet usage (Office for

National Statistics, 2016). Training and devices could also be made available to those who do not use the internet regularly.

Group self-management for fatigue, sleep and pain would also be made available as a Level 2 intervention. This might be more attractive to those who are less familiar with computers and provide further opportunities for face-to-face peer support.

If patients complete a Level 2 intervention and yet still require further support subsequently, or for those who are identified at assessment as needing additional support, Level 3 individual therapy would be offered. Further research is required to determine the ideal way of selecting appropriate individuals at assessment for individual therapy.

Appropriate assessment may mean that these patients can be matched to the appropriate level of care for their individual requirements. However, certain patients who have undertaken symptom management at Level 2, may still require some individual support (Level 3). Again, appropriate assessment following a Level 2 intervention is likely to determine those individuals.

Although different levels of intervention have been proposed, the proposed stepped model of care will support patients to self-manage aspects of their disease, regardless of the level of support that is required for an individual. Self-management programmes should be built on patient perceived problems and should include medical/behavioural management, role management and emotional management tasks (Lorig and Holman, 2003). The bio-psychosocial model (Engel, 1977) addresses these areas and as I mentioned in Chapter 1 (Section 1.5.1), the ICF is based on this model. The concept mapping study (Chapter 3) and the focus groups have identified symptoms which patients want to be able to manage themselves (medical/behavioural management), in order to do the specific things that they want or have to do (role management). The intervention content will be composed of those identified during the clinician validation process in Chapter 4 (see Section 4.4.2). This model of care will also support patients with emotional management by addressing, acknowledging and taking fatigue, sleep and pain symptoms seriously and including CBT and behavioural activation components. Furthermore, the model of care can be expanded in the future to include further options for symptom management including anxiety and depression. These were not included in this early stage of the model as patients did not

identify them as being priorities within the concept mapping study. Furthermore, the focus group study found that patients perceived low mood and worry to be a consequence of these other symptoms. Previous studies have demonstrated that psychological distress correlates highly with pain and fatigue (Segal *et al.*, 2008; Segal *et al.*, 2013). Therefore, by addressing fatigue, sleep and pain within this stepped intervention model, symptoms of anxiety and worry may also improve despite not being directly targeted.

Outcome measures for all symptoms and quality of life, as well as participatory and functional outcomes should be carried out at baseline, at completion of the intervention as well as at follow up, to determine if any changes were sustained. Candidate outcome measures include those which have been specifically designed for the PSS population. These include those measures mentioned in Chapter 1 (Section 1.4) and these are included within the UKPSSR core set of outcome measures. These include individual symptom measures and composite disease and symptom scores. Specific examples of candidate measures to capture the symptoms of fatigue, pain and discomfort include: the Profile of Fatigue and Discomfort (PROFAD) (Bowman *et al.*, 2004) and the ESSPRI (Seror *et al.*, 2011). Patients discussed the impact of their symptoms on their mood during the focus groups, therefore it would be appropriate to capture the symptoms of anxiety and depression with the HADs. Quality of life measures include the SF-36 (Ware and Sherbourne, 1992) and EQ-5D (Brooks *et al.*, 2003), both of which can also be used to calculate the cost effectiveness of an intervention. The SF-36 has the added advantage of being able to measure aspects of function and participation including the ability to both perform daily activities and take on life roles. The Evaluation of Daily Activities Questionnaire is another measure which can be used to measure daily activity ability (Hammond *et al.*, 2014), as this has been shown to be a reliable and valid tool for use with PSS patients (Hammond *et al.*, 2015).

Further candidate outcome measures include those identified through the clinician validation process in Chapter 4 (see Section 4.4.2). Examples of these include activity diaries, sleep diaries, food diaries, activity monitor, Activity Balancing Scale (Dur *et al.*, 2014), the Canadian Occupational Performance Measure (Law *et al.*, 2005b), the Work and Social Adjustment Scale (Mundt *et al.*, 2002), Acceptance and Action Scale II (Bond *et al.*, 2011), the Revised Illness Perception Questionnaire (Moss-Morris *et al.*, 2002) and the Brief COPE (Carver, 1997).

Another measure which might be considered in a future intervention study to improve function and participation is the Institutes for Health funded Patient-Reported Outcomes Measurement Information System (PROMIS®). The PROMIS-29 Profile assesses anxiety, depression, fatigue, pain interference, pain intensity, physical function, sleep disturbance, and ability to participate in social roles and activities. However, it has shown to have large ceiling effects in similar conditions (fibromyalgia, SLE, RA and osteoarthritis) which may limit its responsiveness (Katz *et al.*, 2016).

Appropriate outcome measurement may also help determine patients who may benefit from additional support. Patient activation (the amount of knowledge, skills and confidence a patient has at managing their own health and care) is a concept which can be measured with the Patient Activation Measure (Hibbard *et al.*, 2005). Patients who are highly activated may manage well with a Level 1 or 2 intervention and those who demonstrate low levels of patient activation may benefit from a Level 3 intervention at the outset to avoid 'failing' at a lower intensity intervention. The necessity of failing at a lower level of intervention before being offered the appropriate level of care has been criticised in the UK's stepped care model for anxiety and depression (Richards *et al.*, 2012). Therefore, appropriate assessment at the outset may avoid this problem and ensure the patient is matched to the level of care appropriate for their individual requirements. However, patient activation has not yet been reported in the PSS literature and further research is required to determine whether the Patient Activation Measure would be an appropriate tool to help determine the appropriate level of intervention.

Further investigation will be required to refine the precise intervention content and outcome measures within the stepped care model which has been formed as a result of extensive clinician and patient and family involvement.

7.5.1 Summary

This chapter has summarised the discussions which took place with focus group participants regarding future interventions to support symptom management, with the overall aim of maintaining or improving function and participation in PSS patients. Various modes of delivering interventions were considered and the discussions resulted in a model of care with increasing levels of intensity, which can be stepped up according to individual patient

need. This model will begin to fill the gap which was highlighted in my systematic review of non-pharmacological interventions (Chapter 2).

Chapter 8. Concluding remarks

In this concluding chapter, I review the overall aims and objectives of the thesis, summarise my results, demonstrate how the programme of work presented within this thesis has brought an original contribution of knowledge to the fields of occupational therapy and the management of PSS and suggest areas for future research.

At the beginning of this thesis I cited a person with PSS who said: *'I wake up each day hoping a treatment is developed that will allow me to live an active and normal life again'* (Sjögren's Syndrome Foundation, 2016). During the process of conducting the studies reported within this thesis, I have identified factors preventing people with PSS from being able to live an active and normal life and have addressed them within a proposed model of care. The reported work has started a process, which combined with work from other fields, such as biological sciences, I hope will ultimately make this vision a reality.

My doctoral thesis is built on findings from my previous research. My earlier work demonstrated that many people with PSS experience difficulties with function and participation and that there are few interventions available to support them, despite the obvious need (Hackett *et al.*, 2012a; Hackett *et al.*, 2012b). Although patients experience difficulties with daily function and participation, the reason for these difficulties was not known. The aim of this thesis was to develop a future model of care for PSS.

The objectives were:

1. To determine the effectiveness of any current non-pharmacological interventions for PSS.
2. To collect data from different stakeholder groups to identify priority intervention target areas in PSS.
3. To use existing clinical evidence to establish optimum intervention targets and mechanism of effect of intervention for selected intervention targets.
4. To establish which of these priority areas could realistically be delivered within a UK NHS setting.

The aims and objectives were also published in the protocol for this PhD research in 'BMJ Open' (Hackett *et al.*, 2014) (see Section A.4.1).

To achieve the first objective, I conducted a systematic review of all the published evidence on non-pharmacological interventions. I was particularly interested in the effects of non-pharmacological interventions on participatory or functional outcomes. There were only 8 published studies which fitted the inclusion criteria. The interventions investigated included acupuncture for dry eyes, acupuncture for dry mouth, an intra-oral lubricating device, punctal plugs, silicon hydrogel contact lenses, and psychodynamic therapy. Overall, the quality of most of the included studies was poor and most studies were deemed to be at high risk of bias. Power calculations were not reported for any of the studies and they were likely to be underpowered to detect an effect size that is predicted to be modest. Overall I concluded that the results of the systematic review were inconclusive and there was not enough published evidence to either support or refute non-pharmacological interventions. An earlier version of this review was published in the journal 'Rheumatology' (Oxford) in 2015 (Hackett *et al.*, 2015) (see section A.4.1) and the systematic searches and review were subsequently updated for this thesis.

As the systematic review did not give a clear indication of which direction to take when considering the development of an intervention model; it was important to next determine factors interfering with functional activities and participation. I therefore collected data from different stakeholder groups in order to identify priority factors which were deemed to interfere with function and participation. I used GCM methodology to carry out this study. The stakeholder groups included patients with PSS, adults who lived with someone who has PSS and health care professionals who treat PSS patients. The participants carried out brainstorming, sorting and prioritisation tasks which identified factors interfering with functional activity and participation, grouped these factors into themes and prioritised them for importance. Although the stakeholder groups will have their own unique perspectives on PSS, there was a high level of agreement regarding the priority themes and the individual factors within these themes. Interpretation of the concept maps which resulted from this study, demonstrated that it was a priority for people with PSS to be empowered by being taken seriously and given support to managing their symptoms themselves. Therefore, in theory, by supporting patients to manage their priority symptoms themselves (fatigue, sleep

disturbances and pain), their ability to perform daily activities and participate should improve. This hypothesis needs to be tested in future work.

In order to determine optimum intervention components for these target symptoms, I consulted clinicians working in each of these specialist clinical areas to review statements within the concept maps and to determine which statements could be interventions and those which could be outcomes. This process meant that possible intervention components and outcomes were identified from the original ideas which had previously been generated from people with the lived experience of PSS and from clinicians working with PSS patients. The clinicians also provided specific examples of intervention components and outcome measures.

To explore the lived experience of fatigue, sleep disturbances and pain in PSS further, I conducted focus groups with patients and spouses. Patients explained that these symptoms all interact with each other and if one symptom becomes worse, it seems to affect the others. The experience of symptoms varied between patients and also varied at different times for the same individuals. Patients currently employed a range of strategies to manage these symptoms themselves, but they were not always successful at employing them. They require individual support to manage these symptoms well and would welcome the provision of such interventions. Furthermore, it was apparent that it would be particularly helpful for patients to have accessible support and appropriate information around the time of receiving their PSS diagnosis.

Patients were aware of constraints within the NHS and the focus groups demonstrated that different patients require different levels of support. A future model of care to support patients in the management of fatigue, sleep disturbances and pain symptoms has been proposed. Within this model, all patients will have access to appropriate information and support at diagnosis. Tailored interventions will then be made available to support with symptom management and patients would have choice over which symptom they choose to initially address. This support would be made available digitally with support from a clinician and/or via groups facilitated by a clinician with support from an expert patient. Some patients require a higher level of support and one-to-one face-to-face support would be made available to those individuals who are identified at assessment or those who require additional support following a digital or group intervention.

There are several limitations to this work. The work has resulted in a future model of care and has identified candidate intervention content and outcome measures. There is more work to be done in order to refine the specific intervention content, to pinpoint mechanisms of action and to narrow down identified outcomes to evaluate the resulting interventions within each step of the model. Further qualitative work should also be conducted with PSS patients who work full-time, as this population was not represented in the focus groups and their views need to be represented. Nevertheless, the work contained within this thesis has provided a platform for future research in this area by contributing new knowledge and developing a stakeholder informed model of non-pharmacological symptom management.

This model of care developed in this thesis has focussed on the highest priorities of stakeholders as a result of the concept mapping study. However, other causal pathways which were identified within the maps (see Section 4.4.1.2) also warrant further attention, such as the development of healthcare systems to ensure the implementation of appropriate PSS self-management interventions.

Self-management interventions are behavioural interventions which contain many interacting components (Jonkman *et al.*, 2017). Therefore they are complex (Medical Research Council, 2000). In order to develop and evaluate such complex interventions the MRC has drawn up a Framework as guidance to follow (Craig *et al.*, 2006) (also see Section 1.5.5.1). The work contained within this thesis has been firmly rooted in the development phase of this Framework. I have used a combination of qualitative techniques in order to review of existing evidence and to explore and describe patient experience as recommended in the Framework. As a result, the findings within this thesis have formed a theoretical and empirical basis for the development of a stepped intervention model which targets unmet needs of PSS patients. Within this developmental stage, I have performed key tasks to identify intervention targets and develop an intervention model. In addition, I have begun to explore mechanisms whereby the proposed intervention model will lead to functional change through exploring the lived experience of important symptoms which are deemed to affect ability to perform daily activities and participation in PSS patients. Finally, by involving clinicians who work in the specialist areas of fatigue, sleep and pain, a longlist of outcome measures has been identified.

The programme of research reported within this thesis has established which priority areas could be realistically delivered within a UK NHS setting as I have sought and represented the views of multiple stakeholders from multiple NHS sites. Furthermore, patients and spouses have provided further insights into the appropriate delivery of future services.

Future research should focus on developing the specific content of each level of intervention. This would include recommendations from the upcoming BSR/BHPR Guideline on PSS (Price *et al.*, 2016) and use evidence from similar conditions which have similar symptoms, including fibromyalgia, inflammatory arthritis and SLE. Next, the feasibility and of delivering these interventions should be tested in feasibility studies. If the delivery of the specific intervention components were deemed to be feasible, the efficacy should then be evaluated in multi-site RCTs. Further research is also recommended to determine which patients would benefit most from higher and lower intensity interventions for fatigue, sleep disturbances and pain symptoms.

Future research is needed to develop specific content for interventions at each level of the model, followed feasibility and piloting and multi-site randomised controlled trials to determine effectiveness. If these interventions are deemed to be effective, they should be implemented within an NHS setting, thereby offering patients practical ways of managing their symptoms and improving their quality of life.

Following the work contained within this thesis, I have designed a future programme of work for which I have secured funding. This proposal is to develop the specific content of a Level 2 digital intervention, to co-design the interface with patients and web-developers and to conduct a feasibility study and process evaluation of the intervention. A summary of this proposal can be seen in Appendix 13.

The unique model of intervention development used within this thesis can be replicated in other diseases and offers occupational therapists and other clinicians a practical approach to intervention development which incorporates both theory and stakeholder opinion.

To conclude, the work within this thesis provides a comprehensive understanding of factors which influence daily function and participation in PSS patients. PSS has been an under researched disease, and as a consequence many needs of patients remain unmet within clinical settings. This work presents a stakeholder-informed model for delivering future non-

pharmacological interventions to address stakeholder informed priorities. As such, a model has been developed which will ultimately support patients to manage symptoms of fatigue, sleep disturbances and pain, which are perceived by patients, their families and health professionals to impact on performance of daily activities and participation.

Appendix A.

A.1 Ethical application and approval for concept mapping study

A.1.1 Study protocol

Background

Primary Sjögren's syndrome (PSS) is an autoimmune rheumatic condition affecting between 150,000-250,000 adults in the UK[1,2]. In addition to the classic symptoms of oral and ocular dryness, arthralgia and myalgia[3,4], people with PSS also experience significant fatigue[5,6], autonomic dysfunction[7,8], sleep disturbance, daytime somnolence[9], and a markedly reduced quality of life[10]. Furthermore, PSS is associated with significant direct and indirect healthcare costs[11-12].

We recently conducted a literature review on the impact of PSS on everyday activities and concluded that many PSS patients are restricted in their ability to engage in a wide range of everyday activities[13]. Consistently, using the Improved HAQ®, a validated instrument for assessing functional ability, we demonstrated that people with PSS have significant functional impairment that is comparable to those with chronic fatigue syndrome[14].

Despite their significant functional disability, current medical care for PSS patients has mainly focussed on pharmacological interventions for their classic symptoms, which are at best only partially effective[15]. There is currently no intervention aimed at improving their function or participation in everyday activities. This is in contrast to patients with other long-term conditions such as cancer, chronic fatigue syndrome and chronic pain who have access to psychosocial therapies which have been shown to improve symptoms and functional ability[16-19]. Therefore, there is a large unmet need for the development of effective interventions to improve function for people with PSS.

In order to develop an effective intervention that is deliverable in the NHS, not only should we learn from existing evidence, it is also important for us to understand what the key issues are for the service users, their carers, healthcare professionals and those

who commission and manage NHS services for PSS patients to ensure deliverability of the intervention. The Medical Research Council (MRC) framework for complex intervention development[20] recommends an iterative stepped, structured, mixed-methods approach. At the early stages, when little is known regarding the bio-psychosocial determinates of illness and illness-associated functional capacity, a combination of qualitative techniques to explore and describe patient experience and a review of the existing evidence is recommended. Such findings will then form the theoretical and empirical basis for intervention development and disease model construction. The key tasks at this stage are to identify intervention targets, the mechanisms whereby the proposed intervention will lead to functional change, and a specification of how this change will be measured.

Whilst the MRC guidelines[20] provide a useful framework for complex intervention development, they are less clear on what the modelling of the condition should look like. A variety of methods from economic modelling to computer simulation have been suggested, many of which are not applicable to complex psychosocial interventions. In this regard, concept mapping has been used to good effect for strategic complex planning in other diseases including dementia[21], intervention planning in cancer[22] as well as for designing interventions to prevent work disability in rheumatoid arthritis patients[23] and to understand their work requirements[24].

In this study, we aim to apply group concept mapping to identify priorities and intervention strategies that could improve daily function of people with PSS. Such findings will be used in combination with existing evidence as the basis for the development of an intervention package aimed at improving daily function for people with PSS. If effective, this approach also offers the potential for a portable framework that would introduce some consistency into a currently ad hoc process of complex intervention development.

Aims and Objectives

1. To identify what is of importance to different stakeholder groups regarding priority target areas for an intervention for PSS
2. To establish which of these priorities might be desirable to implement as an intervention

Staff

Katie Hackett, Arthritis Research UK AHP Training Fellow and PhD Student, Newcastle University

Principle Investigator: Professor Wan-Fai Ng, Professor of Rheumatology/Honorary Consultant in Rheumatology, Newcastle University/Newcastle upon Tyne Hospitals NHS Foundation Trust

Professor Julia Newton, Dean of Clinical Medicine/Honorary Consultant in Ageing and Medicine, Newcastle University/ Newcastle upon Tyne Hospitals NHS Foundation Trust

Dr Tim Rapley, Lecturer, Newcastle University

Dr Vincent Deary, Senior Lecturer, Northumbria University

Dr Katherine Deane, Senior Lecturer in Research, University of East Anglia

Research Governance and Sponsorship

Research Sponsorship

The Newcastle upon Tyne Hospitals NHS Foundation Trust is the sponsor of the project and will indemnify the project.

Caldicott guardian approval

Caldicott guardian approval will be obtained for the transfer of personal data (names and addresses of registry patients) between clinicians at Patient Identification Centres and the research team at Newcastle upon Tyne Hospitals NHS Foundation Trust.

Recruitment

Participant identification

The following groups of participants will be invited to take part in the study: Patients who have PSS and are participants of the United Kingdom Primary Sjögren's Syndrome Registry (UKPSSR). Secondly, adults who live with a another adult with PSS, who knows them very well, such as a partner or adult household member who has some insight into how their disease impacts on their life (AHMs). AHMs will be identified by the patient participants. Finally, healthcare professionals from the UKPSSR network and primary care network of North of Tyne (HCPs).

Approaching potential participants

Patients who are part of the UKPSSR have already consented to being invited to participate in further PSS research studies via a written invitation. Local clinicians will provide a member of the research team via a secured nhs.net email account with a password protected spreadsheet containing the names and addresses of UKPSSR patients. The invitations packs will be posted out from Newcastle to participants. The invitation packs will contain an invitation to an adult household member. The patients will be given the option to pass on this invitation to their spouse or another adult who knows how their disease may impact on their life. Staff participants will be approached through email mailing lists, including clinicians who are part of the UKPSSR. These clinicians will be asked to forward the email to members of their teams. GPs will be invited via an email contact list held by North of England Commissioning Support Research and Development Officer, who will forward the email on our behalf. Potential staff participants may be sent reminder emails up to 3 times, with 1-3 weeks between each email. Postal reminders may be sent out twice to potential participants.

Consenting procedures

Participants will be given a consent form and study information sheet with their invitation pack or as attachments to their email invitation, in the case of staff participants. Participants will be provided with the contact details of a research team member and can contact him/her if they have any questions about the study before consenting to take part. All participants are free to withdraw at any time without giving a reason.

Anonymisation procedure

All data collected for this project will be “link anonymised”. Participants will be allocated a code which will be stored on a password protected nhs computer and will only be seen by Ms Hackett who has an honorary NHS contract.

Data handling

Paper documentation will be stored in a locked filing cabinet in a locked room at Newcastle upon Tyne NHS Foundation Trust. Only personnel who are members of the research team, with a contract at Newcastle upon Tyne NHS Foundation Trust will be

given access, on a “need to know” basis and will sign a confidentiality agreement. Data will be stored and treated according to the Data Protection Act 1998.

Summary of project

We will use concept mapping to explore the perspectives of PSS patients, their partners/carers, healthcare professionals and managers involved in their care on what will improve functional capacity of PSS patients. Concept mapping, developed by Trochim [25], is a mixed-methods participatory tool based on a combination of group processes (brainstorming, sorting, rating and group interpretation) and a sequence of multivariate statistical analysis (multidimensional scaling and hierarchical cluster analysis) that generate graphic representations ("Concept Maps") of all stakeholders opinions [30].

Methods

Sample size

We will recruit a minimum of 50 participants to each group, which is recommended for scientific validity[25]. However we will seek to recruit approximately 280 participants in total in order to conduct sub group analyses.

Idea generation/Brainstorming

I will seek open contribution of ideas from each stakeholder group in response to a focus prompt.

Patients with PSS and adults who live with them/adult household members (AHMs) will participate in the concept mapping exercise via one of the following means: (a) face-to-face focus groups of 6-12 people, (b) a web-based interface or (c) paper-based questionnaire. Health care professionals (HCPs) will participate via the online web-based interface or on paper-based questionnaires. Participants completing the web-based concept mapping exercise will be given a unique username (not their name) and password. Baseline demographics will be collected for all participants. The patient group will be asked to complete some relevant validated patient reported outcome measures on mood, quality of life, function, fatigue, dryness, discomfort and pain. AHMs will be asked to complete some short validated questionnaires to measure the impact of their spouse/relative's disease on them, as this may influence their opinion

in the concept mapping exercise, regarding what they feel as priority areas for health care intervention. All participants will be asked to complete the following sentence or focus prompt in these brainstorming sessions:

“A person with primary Sjögren's syndrome would be able to do more of the things they want to do and the things they have to do if.....”

Participants will be asked to think of as many responses as they can during this process. In the face-to-face sessions, a facilitator will record the statements and the participants will see the statements as they evolve. A facilitator may use neutral prompts if ideas start to dry up. Participants also have the option of completing their responses on a piece of paper and handing it to a facilitator if they do not feel comfortable verbalising their responses. In the online format, participants will be able to see the anonymous responses of participants who have already completed the brainstorming process, which may help to prompt their own ideas.

Ideas analysis

All statements will be analysed and synchronised by the Study Advisory Group consisting of representatives of all stakeholder groups, myself and the research team. We will use a structured process recommended by Kane and Trochim[26] to remove duplicate statements and to ensure wording is clear. This will condense the statement set to one which is of manageable size (≤ 96 statements[25]) for the subsequent sorting and rating exercise but large enough to ensure saturation of the topic[25,27].

Sorting and rating

All participants who have previously taken part in the brainstorming exercise will be invited to take part in the sorting and rating phase. Some participants may be recruited solely to the sorting and rating phase if saturation of the brainstorming topic is achieved prior to recruiting 300 participants or if there is significant participant attrition between the separate phases of the study. Participants will be asked to rate each statement in the distilled statement set for importance and feasibility on a 5 point rating scale, and to sort the statements into themes or groups of similar statements or ideas. Participants may choose a different method to sort and rate to the one they chose for brainstorming if they wish, for example, complete the sorting

and rating exercise online if they attended a face-to-face meeting for brainstorming and vice versa.

Concept mapping analysis and interpretation

The data generated from the above exercises will be analysed and represented in objective form as visual maps using the Concept Systems Global© software package.

The maps will highlight the priority areas for each stakeholder group in improving function of PSS patients. Similarities and disparities between the stakeholder groups can be identified and if appropriate, subgroup analysis can be carried out using the baseline demographic data collected at the start of the study. The “go zones” represent areas that are of most importance for more than one stakeholder group and so are of particular importance for planning interventions.

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A.1.2 Participant information sheet

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Freeman Road
Newcastle upon Tyne
NE7 7DN
Tel: 0191 2228125
E-mail: Katie.Hackett@ncl.ac.uk

Participant Information Sheet

Research study: Developing service user informed interventions for primary Sjögren's syndrome (PSS) [REC Ref: 13/NI/0190]

Summary Information

This front sheet gives you summary information about the research study that you are being invited to take part in. More details can be found in the following pages.

- You are being invited to take part in a research study which we hope will provide us with information to help develop an intervention for PSS
- We are involving three stakeholder groups in this study; adults with PSS; adults who live with someone with PSS and health care professionals involved in caring for people with PSS
- There are three ways you can take part in the study;
 - a) If you live within a 10 mile radius of Newcastle, you can choose to attend two separate face-to-face group meetings with other participants who have PSS
 - b) By participating in two separate online questionnaire based exercises, or
 - c) By completing questionnaires on two occasions by post
- You will be asked to complete two exercises. On the first occasion, you will be asked to participate in a brainstorming exercise and to individually complete some questionnaires. On the second occasion, you will be asked to individually prioritise some statements and sort them into themes.

We are inviting you to take part in a research study. Before you decide, you need to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear to you or if you would like more information. We can be contacted on the telephone number at the end of this sheet. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

The main treatment currently available to people with primary Sjögren's syndrome (PSS) is relatively limited. Medical interventions can help with relieving some symptoms, but many people with PSS still have difficulties which can result in reducing their ability to participate fully in many everyday activities.

In this study we will explore the specific difficulties that people with PSS have which impact on their ability to fully participate in the activities that they would like to do. To do this, we will collect information from adults with PSS, spouses or other adults who live with them and healthcare professionals who are experienced in managing PSS. The results of this study will help us to design a treatment program to help enable people with PSS to participate more fully in their preferred daily activities.

Why have I been invited?

You have been invited to participate in this study because you have a diagnosis of PSS.

Are there any inclusion or exclusion criteria?

We are seeking to recruit participants who have a confirmed diagnosis of primary Sjögren's syndrome. These people should be aged 18 years or over.

Do I have to take part?

Participation in this study is entirely voluntary. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time without giving a reason.

What will happen to me if I take part?

There are 3 ways you can take part in this study. Please indicate your choice on the reply form and return it with the signed consent form.

Option A (Face-to-face group meetings)

If you live within a 10 mile radius of Newcastle, you may participate in the face-to-face meetings. You will be asked to attend 2 meetings which will take place during the next 9 months at the Freeman Hospital in Newcastle. The meetings involve informal discussions among a group of 8-15 people who have PSS. Each meeting will last approximately 60-90 minutes. There will be a break during both meetings and refreshments will be provided. The group meetings will be run by two researchers, Kate Hackett and Dr Tim Rapley.

In the first meeting you will be asked to individually complete some questionnaires about yourself. Following this, the group will be asked to consider the following question:

“People with primary Sjögren’s syndrome could do more of the things they want to do or have to do if.....”.

The discussion will be tape-recorded and suggestions by the group will be written on flip charts. You will also have a note pad on which you can individually write your statements, rather than share with the group if you wish. There is no pressure on any individual to make any suggestions and any information you provide during the meeting will be kept anonymous.

In the second meeting, the group will be asked to look at the suggestions that were generated by all three participant groups (people with primary Sjögren’s syndrome, adult household members and health care professionals) during the first meetings. There will be up to 80-100 statements or suggestions. You will be asked to rate each statement or suggestion using a scoring system for importance and for feasibility. You will also be asked to group the statements or suggestions into themes.

Option B (Online participation)

If you have access to a computer with internet access, you can complete the exercises described in option A online. You will be given the web address and be allocated a unique username and password for you to complete the exercises in your own time, like in the face-to-face option. You will need to do this on two separate occasions for the two parts of the study. You will be contacted when the second part of the study is ready for you to take part.

When you log on to the website for the first time, you will be asked to complete some questions about yourself. Next, you will be asked to consider the following question:

“People with primary Sjögren’s syndrome could do more of the things they want to do or have to do if.....”.

You will be asked to record as many responses to this statement as you can think of. There will be some responses available for you to see from people who have completed the exercise before you. It is not possible for you or the researchers to see who has recorded which answer, (i.e. your responses will be completely anonymous). If you think of more replies after you have completed the exercise, you can log back in again and add further statements, providing it is before the first part of the study has been completed. Overall we anticipate the first exercise taking 10-60 minutes to complete, depending on how many responses you provide. When we send out your username and password, we will enclose some additional questionnaires for you to complete and return in a prepaid envelope. We anticipate these taking up to 20 minutes to complete.

You will then be contacted via telephone, letter or email at a later date to complete the second exercise. If you are logging on for the first time, (if you did not take part in the first part) you will first be asked to complete some questions about yourself. In the second exercise, you will be presented with a list of responses which have been produced by all participants in the first exercise. There will be around 80-100 statements. You will be asked to rate each statement using a scoring system for importance and for feasibility. You will also be asked to group the statements into themes. Again, you will be able to log onto the interface on more than one occasion if this is easier for you. We anticipate this taking between 1 and 1.5 hours to complete.

Option C (Questionnaire-based, by post)

You will be sent some questionnaires about yourself which we will ask you to complete. You will also be asked to consider the following question:

“People with primary Sjögren’s syndrome could do more of the things they want to do or have to do if.....”

You will be asked to record as many responses to this statement as you can think of and to return the completed forms in the prepaid envelope within two to three weeks of receiving them. We anticipate this exercise will take 30-60 minutes to complete.

For the second exercise, we will contact you again by post. We will enclose a set of replies from the first exercise. There should be about 80-100 statements. You will be asked to rate each statement using a scoring system for importance and for feasibility. You will also be asked to group the statements into themes. We anticipate this taking 1 hour to 90 minutes to complete. However, you do not have to complete the exercise all in one go and you can do it over several sessions if this is easier for you. Again, you will be asked to return the completed forms in a prepaid envelope to us.

Expenses and payments

There is no payment for your participation in this study. We will refund your travel expenses if you attend the face-to-face meetings.

What are the possible benefits of taking part?

There is no direct benefit for your participation, however the information we get from the study will help us to develop an intervention to improve the daily lives of people with primary Sjögren's syndrome.

Once I take part, can I change my mind?

You can withdraw at any time and you do not have to explain the reason why you have decided to withdraw. Simply let us know of your decision using the contact details provided.

What if I lose the ability to consent to taking part during the study?

The research team would retain any non-identifiable data that you had already provided.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Kate Hackett, can be contacted by telephone: 0191 2228125. If you remain unhappy and wish to complain formally, you can do this by contacting Kate's academic supervisor, Dr Wan-Fai Ng, by telephone 0191 2223449. Alternatively, you can write to us at the address below.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Newcastle University but you may have to pay your legal costs.

If the research team are concerned about your health after reviewing your responses in the questionnaire pack, we may contact your consultant or GP to ensure you are receiving appropriate support.

Will my taking part in this study be kept confidential?

Yes. All information collected about you during the course of this study will be kept strictly confidential. Your personal details, such as your name and address, will be recorded and stored anonymously according to the Data Protection Act (1998). Your name will be substituted by a coded reference number so that your information cannot be traced back to you. Paper documents which contain your personal data will be stored in a locked cabinet in a locked room at Newcastle Hospitals NHS Foundation Trust. Paper documents will be shredded six months after the end of this study. Anonymised electronic data (i.e. without your personal information) will be stored securely on the password protected web based interface and on a password protected computer at Newcastle Hospitals NHS Foundation Trust for fifteen years. After this, all data will be deleted. Data will only be viewed by the research team. If the data collected in this study is used in a written report, such as a thesis or published paper, we will not use your name or personal details.

What will happen to the results of the study?

The results of this study can be used to develop an intervention to help people with PSS to do more of the activities they want to or have to do. We hope it will in turn improve the quality of life of many people with PSS as well as reducing the cost of healthcare.

We aim to publish the results of this study in a report for Arthritis Research UK (the funder of this study) in scientific journals and the study will be used as part of a written PhD thesis.

Who is organising and funding the research?

This study is part of a research project funded by Arthritis Research UK. The main researcher is Arthritis Research UK Training Fellow, Kate Hackett. Kate will work under the supervision of Professor Wan-Fai Ng (Newcastle University) Professor Julia Newton (Newcastle University), Dr Tim Rapley (Newcastle University) and Dr Vincent Deary (Northumbria University).

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Office for Research Ethics Committees, Northern Ireland. In addition, the research study has been reviewed by relevant research governance bodies at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University.

Reminder letters

Reminder letters may be sent to people who have not responded to the invitation to participate.

Further information and contact details:

Please do not hesitate to contact us if you need further information about this study:

Kate Hackett, Arthritis Research UK Training Fellow
Musculoskeletal Research Group, 4th Floor Catherine Cookson Building
Faculty of Medical Sciences
Newcastle University
Newcastle upon Tyne
NE2 4HH
Tel: 0191 2228125
E-mail: katie.hackett@ncl.ac.uk

Advice as to whether you should participate:

If you have any general queries about participating in research you can contact the hospital's Patient Advisory and Liaison Service (PALS). General information is also available on the Involve website (www.invo.org.uk). **INVOLVE** is a national advisory Group, funded by the Department of Health, which supports active public involvement in NHS, public health and social care research.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the Newcastle University but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Finally

Many thanks for considering taking part. Please keep this information sheet. We will ask you to sign a consent form if you agree to take part and we will give you a copy of this to keep.

Thank you for taking your time to read this information sheet. Please complete and return the enclosed reply slip in the envelope provided if you would like to participate in this study.

The Newcastle upon Tyne Hospitals

NHS Foundation Trust

Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
NE1 4LP

Tel: 0191 233 6161
Fax: 0191 201 0155

Research study: Developing service user informed interventions for primary Sjögren's syndrome [Ethics reference number to go here]

CONSENT FORM

Name of researcher: Kate Hackett

Please INITIAL each box

1. I confirm that I have read and understand the information sheet dated 14/05/13 (Ref PIS/Pt Version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that data collected during the study may be looked at by members of the research team at the Newcastle University and the UK Primary Sjogren's Syndrome Registry research team at Newcastle Hospitals NHS Foundation Trust and individuals from regulatory authorities and the NHS Trust where it is relevant for my taking part in the research. I give permission for these individuals to access my information. ☐
4. I understand that if I attend a focus group meeting, this will be audiotaped and that subsequently this will be transcribed and anonymised and the tape will be destroyed ☐
5. I agree to take part in the above study ☐

Name of patient Date Signature

Name of researcher taking consent Date Signature

when completed: 1 for patient: 1 for researcher;

A.1.4 Letter providing favourable ethical approval



Office for Research Ethics Committees Northern Ireland (ORECNI)

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HSC REC 3

03 December 2013 **CORRECTED 30 DECEMBER 2013**

Professor Wan-Fai Ng
Professor of Rheumatology
Musculoskeletal Research Group, ICM, 4th Floor
Catherine Cookson Building, The Medical School
Newcastle University
Framlington Place
Newcastle upon Tyne
NE2 4HH

Dear Professor Ng

Study title: Developing a service user informed bio-psychosocial intervention
for primary Sjogren's syndrome using group concept mapping.
REC reference: 13/NI/0190
IRAS project ID: 125562

Thank you for your letter of 25 November 2013, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Miss Jan Daley, jan.daley@hscni.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The documents reviewed and approved by the Committee are:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Advertisement GP/Email/invite	1	30 May 2013
Covering Letter Professor W Ng		19 September 2013
Covering Letter Online/BrStm	1	21 May 2013
Covering Letter Email, Ms K Hackett		27 November 2013
Evidence of insurance or indemnity Zurich Municipal, University of Newcastle Policy number NHE-08CA03-0013		26 July 2013
Interview Schedules/Topic Guides Face to Face Meetings Guide	1	21 November 2013
Investigator CV Professor Ng	1	18 October 2013
Investigator CV Ms K Hackett	1	23 September 2013
Letter from Sponsor IRAS signed by Mr S Scott		25 October 2013
Letter of invitation to participant Pt	2	13 November 2013
Letter of invitation AHM	2	13 November 2013
Other: Investigator CV, Professor J Newton	1	23 September 2013
Other: Investigator CV, Professor T Rapley	1	23 September 2013
Other: Investigator CV, Dr V Deary	1	23 September 2013
Other: Peer Review, Arthritis Research UK	1	31 October 2013
Other: Letter of Award, Arthritis Research UK	1	14 January 2013
Other: Advertisement, Poster	1	21 June 2013
Other: Reply/HCP	1	21 May 2012
Other: Reply/AHM	1	22 May 2012
Other: Reply/Pt	1	21 May 2012
Other: Covering Letter, Online/SortRate	1	21 May 2013
Other: Covering Letter, Fgp/Brnstorm	1	23 May 2013
Other: Covering Letter, Fgp/SortRate	1	23 May 2013
Other: Covering Letter, Post/Brstm	1	21 May 2013
Other: Covering Letter, Postal/Sortrate	1	21 May 2013
Other: Advertisement, HCP/Email/invite	1	30 May 2013
Other: Reminder/Online/SRate	1	21 May 2013
Other: Reminder/Online/BrStm	1	21 May 2013
Other: Reminder/Postal/BrStm	1	21 May 2013
Other: Reminder/Postal/SRate	1	21 May 2013
Other: Rating Recording Sheet	1	21 November 2013
Other: Sort Recording Sheet	1	21 November 2013
Other: Invite/HCP	2	13 November 2013
Participant Consent Form: Pt	1	31 May 2013
Participant Consent Form: AHM	1	31 May 2013
Participant Consent Form: HCP	1	31 May 2013

Participant Information Sheet: HCP	2	13 November 2013
Participant Information Sheet: SortRateHCP	2	13 November 2013
Participant Information Sheet: AHM	2	13 November 2013
Participant Information Sheet: SortRate AHM	2	13 November 2013
Participant Information Sheet: SortRatePt	2	13 November 2013
Participant Information Sheet: Pt	2	13 November 2013
Protocol	1	29 July 2013
Questionnaire: AHM	1	25 November 2013
Questionnaire: Excel spreadsheet		
Questionnaire: Patients	1	25 November 2013
REC application		24 October 2013
Response to Request for Further Information Covering letter, Professor Wan-Fai Ng		25 November 2013
Summary/Synopsis Flowchart	1	24 June 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/NI/0190

Please quote this number on all correspondence

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

With the Committee's best wishes for the success of this project.

Yours sincerely


Dr Hilary Russell
Chair

Email: jan.daley@hscni.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: Mr Sean Scott
Joint Research Office
Leazes Wing
Royal Victoria Infirmary
Newcastle upon Tyne NHS Foundation Trust
Queen Victoria Road
Newcastle
NE1 4LP

A.2 Substantial amendment to previous ethical application

A.2.1 Amendment to previous study protocol

The following substantial amendment was added to the previous protocol (see Section A.1.1) and resubmitted to the ethical board, in order to gain appropriate approvals to conduct the focus groups.

Developing the intervention

We will identify where each priority factor from the GCM exercises fits within the World Health Organisation International Classification of Functioning Disability and Health (ICF) framework [1]. Key priority factors will be targeted for a proposed intervention to improve daily function and participation for PSS patients.

First, potential intervention techniques or ‘active ingredients’ will be identified from existing literature and relevant evidence-based theories. These will be identified in relation to each priority factor identified in the concept mapping exercise. Second, the factor is specified as an observable and measurable ‘construct’ and a measure for identifying change in it will be selected. Third, each technique and barrier pair is presented as a testable hypothesis with function and participation as the ultimate outcome.

An illustrative example of the application of this three-step method are shown below.

Illustrative example: Potential factor: Chronic fatigue

Evidence based intervention techniques to target chronic fatigue include, grading physical activity/exercise [2] and goal setting, biofeedback and body changes [3]. Chronic fatigue is commonly measured as the self-reported mental and physical tiredness, by using tools such as the Chalder Fatigue Scale [4] or the Profile of Fatigue [5]. The testable hypothesis may be articulated as “grading, goal setting, biofeedback and body changes can be used to reduce chronic fatigue in order to increase participation in meaningful occupations.”

Focus Groups

Once the potential intervention techniques have been identified from the literature, these will be presented to people with PSS, their carers and occupational therapists in

focus groups. The focus groups will provide opportunities to gather feedback regarding the specific intervention techniques, how the techniques will be best delivered and measures of effectiveness. Participants will be asked to generate ideas regarding how to deliver the techniques in an effective and acceptable way. Patient and carer participants will be identified from a regional specialist medical service for PSS and will be those who have previously indicated an interest at being involved with further research. Potential therapist participants will be recruited from local hospitals and community based occupational therapists.

Focus group participants will also be invited to comment on the proposed outcome measures, including the choice of instrument(s) and the processes of administering and completing these instrument(s). The results will be used to refine the intervention package.

References

1. Thomas E, Hay EM, Hajeer A, Silman AJ. Sjogren's syndrome: a community-based study of prevalence and impact. *Br. J. Rheumatol.* 1998;37(10):1069-76.
2. Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. *Arthritis Res Ther* 2009;11(3):229.
3. Fox RI. Sjogren's syndrome: current therapies remain inadequate for a common disease. *Expert opinion on investigational drugs* 2000;9(9):2007-16.
4. Fox RI. Sjogren's syndrome. *Lancet* 2005;366(9482):321-31.



Clinical Research Facility,
Royal Victoria Infirmary
Queen Victoria Road,
Newcastle upon Tyne
NE1 4LP
Tel: 0191 2228125
E-mail: Katie.Hackett@ncl.ac.uk

Participant Information Sheet

Research study: Developing service user informed interventions for primary Sjögren's syndrome (PSS) [REC Ref: 13/NI/0190]

Summary Information

This front sheet gives you summary information about the research study that you are being invited to take part in. More details can be found in the following pages.

- You are being invited to take part in a research study which we hope will provide us with information to help make improvements to an intervention for PSS
- We are involving three stakeholder groups in this study; adults with PSS; adults who live with someone with PSS and health care professionals who could potentially deliver an intervention for people with PSS in the future
- You are being asked to take part in a focus group to discuss a proposed intervention which has been developed for people with primary Sjögren's syndrome. We will seek your opinions about the intervention and ask if you have any suggestions to improve both the content and mode of delivery.

We are inviting you to take part in a research study. Before you decide, you need to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear to you or if you would like more information. We can be contacted on the telephone number at the end of this sheet. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

The main treatment currently available to people with primary Sjögren's syndrome (PSS) is relatively limited. Medical interventions can help with relieving some symptoms, but many people with PSS still have difficulties which can result in reducing their ability to participate fully in many everyday activities.

We have recently explored the specific difficulties that people with PSS have which impact on their ability to fully participate in the activities that they would like to do. We have collected information from adults with PSS, spouses or other adults who live with them and healthcare professionals who are experienced in managing PSS. This has helped us design a treatment program to help enable people with PSS to participate more fully in their preferred daily activities.

Why have I been invited?

You have been invited to participate in this study because you either have a diagnosis of PSS, live with someone with PSS or are a health care professional who may deliver the intervention in the future.

Are there any inclusion or exclusion criteria?

PSS patients should be 18 years or older and have a confirmed diagnosis of primary Sjögren's syndrome. Spouses or adults living with someone with PSS should be over 18. Health care professionals do not need to have experience of working with patients with PSS.

Do I have to take part?

Participation in this study is entirely voluntary. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time without giving a reason.

What will happen to me if I take part?

You will be asked to attend a focus group of up to 10 people which will take place during the next 9 months at the Freeman Hospital in Newcastle or at Newcastle University. The meetings involve informal discussions among a group of 6-10 people and will last approximately 90 minutes. There will be a break during the meeting and refreshments will be provided. The group meetings will be run by two researchers, Kate Hackett and Dr Niina Kolehmainen or Dr Lisa Robinson.

We will present the results of an earlier phase in this study. This was a concept mapping exercise where we sought opinions from patients with PSS, their family members and health care professionals regarding what they thought prevented people from PSS from doing everyday activities. We will then show you an intervention package we have developed based on the most important factors identified from the previous concept mapping exercise. We may also discuss with you training materials we have developed to teach health care

professionals how to deliver the intervention and some measures we have selected to measure any changes in health status following an intervention being used with people with PSS.

The discussion will be tape-recorded and suggestions by the group will be written on flip charts. You will also have a note pad on which you can individually write your ideas or opinions rather than share with the group if you wish. There is no pressure on any individual to make any suggestions and any information you provide during the meeting will be kept anonymous.

Expenses and payments

There is no payment for your participation in this study. We will refund your travel expenses if you attend the face to face meetings.

What are the possible benefits of taking part?

There is no direct benefit for your participation, however the information we get from the study will help us refine an intervention package to improve the daily lives of people with primary Sjögren's syndrome.

Once I take part, can I change my mind?

You can withdraw at any time and you do not have to explain the reason why you have decided to withdraw. Simply let us know of your decision using the contact details provided.

What if I lose the ability to consent to taking part during the study?

The research team would retain any non-identifiable data that you had already provided.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Kate Hackett, can be contacted by telephone: 0191 2228125. If you remain unhappy and wish to complain formally, you can do this by contacting Kate's academic supervisor, Dr Wan-Fai Ng, by telephone 0191 2223449. Alternatively, you can write to us at the address below.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Newcastle University but you may have to pay your legal costs.

If the research team are concerned about your health after reviewing your responses in the questionnaire pack, we may contact your consultant or GP to ensure you are receiving appropriate support.

Will my taking part in this study be kept confidential?

Yes. All information collected about you during the course of this study will be kept strictly confidential. Your personal details, such as your name and address, will be recorded and stored anonymously according to the Data Protection Act (1998). Your name will be substituted by a coded reference number so that your information cannot be traced back to you. Paper documents which contain your personal data will be stored in a locked cabinet in

a locked room at Newcastle Hospitals NHS Foundation Trust. Paper documents will be shredded six months after the end of this study. Anonymised electronic data (i.e. without your personal information) will be stored securely on the password protected web based interface and on a password protected computer at Newcastle for fifteen years. After this, all data will be deleted. Data will only be viewed by the research team. If the data collected in this study is used in a written report, such as a thesis or published paper, we will not use your name or personal details.

What will happen to the results of the study?

The results of this study can be used to refine an intervention to help people with PSS to do more of the activities they want to or have to do. We hope it will in turn improve the quality of life of many people with PSS as well as reducing the cost of healthcare.

We aim to publish the results of this study in a report for the United Kingdom Occupational Therapy Research Foundation (the funder of this study) in scientific journals and the study will be used as part of a written PhD thesis.

Who is organising and funding the research?

This study is part of a research project funded by the United Kingdom Occupational Therapy Research Foundation and Arthritis Research UK. The main researcher is Arthritis Research UK Training Fellow, Kate Hackett. Kate will work under the supervision of Professor Wan-Fai Ng (Newcastle University) Professor Julia Newton (Newcastle University), Dr Tim Rapley (Newcastle University) and Dr Vincent Deary (Northumbria University).

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by _____ Research Ethics Committee. In addition, the research study has been reviewed by relevant research governance bodies at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University.

Reminder letters

Reminder letters may be sent to people who have not responded to the invitation to participate.

Further information and contact details:

Please do not hesitate to contact us if you need further information about this study:

Kate Hackett, Arthritis Research UK Training Fellow
Musculoskeletal Research Group, 4th Floor Catherine Cookson Building
Faculty of Medical Sciences
Newcastle University
Newcastle upon Tyne
NE2 4HH
Tel: 0191 2228125
E-mail: katie.hackett@ncl.ac.uk

Advice as to whether you should participate:

If you have any general queries about participating in research you can contact the hospital's Patient Advisory and Liaison Service (PALS). General information is also available on the Involve website (www.invo.org.uk). INVOLVE is a national advisory Group, funded by the Department of Health, which supports active public involvement in NHS, public health and social care research.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the Newcastle University but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Finally

Many thanks for considering taking part. Please keep this information sheet. We will ask you to sign a consent form if you agree to take part and we will give you a copy of this to keep.

Thank you for taking your time to read this information sheet. Please complete and return the enclosed reply slip in the envelope provided if you would like to participate in this study.

A.2.3 Consent form

Research study: Developing service user informed interventions for primary Sjögren's syndrome [REC Ref: 13/NI/0190]

CONSENT FORM

Name of researcher: Kate Hackett

Please INITIAL each box

1. I confirm that I have read and understand the information sheet dated 15/07/14 (Ref PIS/Refine FGP Version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that data collected during the study may be looked at by members of the research team at the Newcastle University and the UK Primary Sjögren's Syndrome Registry research team at Newcastle Hospitals NHS Foundation Trust and individuals from regulatory authorities and the NHS Trust where it is relevant for my taking part in the research. I give permission for these individuals to access my information. ☐
4. I understand that if I attend a focus group meeting, this will be audiotaped and that subsequently this will be transcribed and anonymised and the tape will be destroyed ☐
5. I agree to take part in the above study ☐

Name of participant Date Signature

Name of researcher Date Signature
taking consent

when completed: 1 for participant: 1 for researcher;

A.2.4 Substantial amendment approval letter



**Office for Research Ethics Committees
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HSC REC B

29 August 2014

Professor Wan-Fai Ng
Professor of Rheumatology
Newcastle University
Musculoskeletal Research Group, ICM, 4th Floor
Catherine Cookson Building, The Medical School
Newcastle University
Framlington Place
Newcastle upon Tyne
NE2 4HH

Dear Professor Ng

Study title:	Developing a service user informed bio-psychosocial intervention for primary Sjogren's syndrome using group concept mapping.
REC reference:	13/NI/0190
Amendment number:	Substantial Amendment #1
Amendment date:	29 July 2014
IRAS project ID:	125562

The above amendment was reviewed at the meeting of the Sub-Committee held on 27 August 2014.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering letter on headed paper		29 July 2014
Letters of invitation to participant	V2	13 November 2013
Notice of Substantial Amendment (non-CTIMP)		29 July 2014
Other [Reply Form Refinement Focus Group]	V1	15 July 2014

Providing Support to Health and Social Care

Other [Email from K Hackett]		29 July 2014
Other [Recruitment email]	V1	15 July 2014
Other [Refinement Focus Group Plan]	V1	15 July 2014
Participant consent form [Refine Focus Group]	V1	15 July 2014
Participant information sheet (PIS) [Focus Group]	V1	15 July 2014
Research protocol or project proposal	V2	15 July 2014

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

13/NI/0190:	Please quote this number on all correspondence
-------------	--

Yours sincerely

Jane Keenan

PP

Ms Sue Trouton
Chair

E-mail: jane.keenan@hscni.net

Enclosures: List of names and professions of members who took part in the review

Copy to: Mr Sean Scott, Newcastle upon Tyne NHS Foundation Trust

HSC REC B

Attendance at Sub-Committee of the REC meeting on 27 August 2014

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Mr John Edward Mone	Retired (Former Executive Director of Nursing)	Yes	
Ms Sue Trouton	Community Midwifery Sister	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Miss Jane Keenan	REC Manager

A.3 Numbered statements within the concept maps

The following table lists each of the numbered statements from within the concept maps.

A person with Sjögren's could do more of the things they want to do or have to do (they).....

1. Know who to contact when their symptoms flare up
2. Have access to a range of good drug treatments
3. Did not have mouth sores or ulcers
4. Knew the range of available treatment options
5. Could go out in the sun
6. They have a good diet
7. There were "one stop" Sjögren's clinics with all relevant health care professionals available
8. Were less prone to getting infections
9. Have access to physiotherapy
10. Were less stressed or worried
11. Have Sjögren's advice leaflets
12. There were appropriate aids and adaptations in the community
13. There was more good research to understand the underlying causes
14. Have professional support during a flare up of symptoms
15. Can see a consultant when needed
16. There was education about Sjögren's for the general public
17. There was education about Sjögren's for people who fund services
18. Were less fatigued
19. Could come to terms with their symptoms
20. There was more good research to test and develop treatments
21. Feel in control of their symptoms
22. Look after their physical, emotional and spiritual wellbeing
23. Felt a family member or supporter could be included in their care planning
24. Have confidence to seek advice when needed
25. Have support to manage their symptoms themselves
26. Their vagina was less dry
27. Their skin was less dry
28. Have access to psychological support
29. There was a cure
30. Could continue to drive
31. Skin problems were treated
32. Their vision was not impaired

A person with Sjögren's could do more of the things they want to do or have to do (they).....

33. Friends and family include them in events
34. Swallowing was easier
35. Public spaces were more Sjögren's friendly e.g. heated/lit/airconditioned differently
36. Didn't have sexual problems
37. There was education on Sjögren's for patients
38. Could access support to help set personal goals
39. Have a disabled parking badge
40. Have an individualised treatment plan
41. Have supportive family and friends
42. Have assistance with shopping, cleaning etc.
43. Have a positive attitude
44. There were diaries for recording symptoms and problems to bring to appointments with health care professionals
45. There was better management of the side effects of drugs
46. They have better mobility
47. Exercise regularly
48. Have access to appropriate aids and adaptations in their homes
49. Could improve their concentration
50. Have less pain
51. There was education on Sjögren's for family members
52. Their mood was better
53. There was education on Sjögren's for healthcare professionals
54. There is good communication between clinicians
55. Could easily describe Sjögren's to others
56. Health care professionals would raise sensitive topics (e.g. sex and vaginal dryness) during consultations
57. Professionals could direct them to support groups and charities
58. Take their medication as prescribed
59. Have support with memory and concentration difficulties
60. Have access to support and advice from other people with Sjögren's
61. Their eyes were more comfortable
62. Have access to a specialist nurse
63. Could come to terms with their limitations

<i>A person with Sjögren's could do more of the things they want to do or have to do (they).....</i>	
64.	Employers were aware of things they could do in the workplace that are helpful for people with Sjögren's
65.	Learn to balance their activity and rest
66.	There was more funding for specialist rheumatology services
67.	Felt a family member or supporter would be welcome at their appointments
68.	Have healthy teeth and/or comfortable dentures
69.	Their throat was less dry
70.	Have access to occupational therapy
71.	Were able to sleep better
72.	Gastrointestinal (stomach and bowel) problems were managed
73.	Public transport was accessible
74.	Were less breathless
75.	There was information available on exercise and Sjögren's
76.	Fatigue was better managed/treated
77.	Have more feeling in their mouth and lips
78.	Have help with dental costs
79.	Diagnosis was quick
80.	Felt they were being taken seriously
81.	Have access to hydrotherapy
82.	Mouth and lips were less dry
83.	Family could understand the symptoms
84.	Their eyes were less dry
85.	Associated conditions are diagnosed and treated
86.	On a bad day people could tell by looking at them how they are feeling
87.	Those unable to work and/or needed support to function, were eligible for benefits
88.	Have access to complementary therapies or alternative remedies
89.	Develop good coping strategies
90.	Keep their body active
91.	Keep their mind active
92.	Were taught relaxation techniques
93.	Their healthcare is better coordinated
94.	Can explain to others what they can and cannot do

Table A-1 The numbered statements within the concept maps

A.4 Publications during my PhD studies

Full texts are provided of first author peer-reviewed publications. I provide references of other papers which I have co-authored or which were published in non-peer reviewed journals.

A.4.1 First author peer-reviewed publications

Hackett, K.L., Gotts, Z., Ellis, J., Deary V., Rapley, T., Ng W-F., Newton, J.L., Deane, K.H.O. (2016) 'An investigation into the prevalence of sleep disturbances in primary Sjögren's syndrome: A systematic review of the literature' *Rheumatology (Oxford)* (doi: 10.1093/rheumatology/kew443 First published online: December 24, 2016).

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An investigation into the prevalence of sleep disturbances in primary Sjögren's syndrome: a systematic review of the literature

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Abstract

Objectives. To identify whether sleep disturbances are more prevalent in primary SS (pSS) patients compared with the general population and to recognize which specific sleep symptoms are particularly problematic in this population.

Methods. Electronic searches of the literature were conducted in PubMed, Medline (Ovid), Embase (Ovid), PsychINFO (Ovid) and Web of Science and the search strategy registered *a priori*. Titles and abstracts were reviewed by two authors independently against a set of prespecified inclusion/exclusion criteria, reference lists were examined and a narrative synthesis of the included articles was conducted.

Results. Eight whole-text papers containing nine separate studies met the inclusion criteria and were included in the narrative analysis. Few of these studies met all of the quality assessment criteria. The studies used a range of self-reported measures and objective measures, including polysomnography. Mixed evidence was obtained for some of the individual sleep outcomes, but overall compared with controls, pSS patients reported greater subjective sleep disturbances and daytime somnolence and demonstrated more night awakenings and pre-existing obstructive sleep apnoea.

Conclusions. A range of sleep disturbances are commonly reported in pSS patients. Further polysomnography studies are recommended to confirm the increased prevalence of night awakenings and obstructive sleep apnoea in this patient group. pSS patients with excessive daytime somnolence should be screened for co-morbid sleep disorders and treated appropriately. Interventions targeted at sleep difficulties in pSS, such as cognitive behavioural therapy for insomnia and nocturnal humidification devices, have the potential to improve quality of life in this patient group and warrant further investigation.

Key words: Sjögren's syndrome, systematic review, sleep, quality of life, disability evaluation

Rheumatology key messages

- Sleep disturbances are common in primary SS patients and should be identified and treated appropriately.
- Interventions targeted at sleep difficulties in primary SS warrant further investigation.

Introduction

Primary SS (pSS) is a systemic autoimmune disease characterized by sicca symptoms [1]. Extraglandular

features are commonly seen in pSS patients, including fatigue [2], orthostatic intolerance [3], pain [4] and depression [5]. These patients commonly experience impaired function [6] and poor health-related quality of life [8]. Fatigue is seen in 75% of patients with pSS [7], is strongly correlated with poor quality of life [8–10] and is associated

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with functional impairment [6]. Due to the prevalence and impact of fatigue, there has been much research into factors associated with this symptom, including potential genetic associations [11] and anti-inflammatory mechanisms [12]. Sleep disturbances have also been reported in the pSS literature [13] and are associated with fatigue [2]. In the general population, impaired sleep is associated with adverse health outcomes including weight gain, depression, pain, impaired immune function, impaired functional performance, increased risk of early mortality and cognitive symptoms such as increased errors and increased risk of accidents [14]. Current recommendations are that adults should regularly have between 7 and 9 h of sleep consistently per night [14].

Many sleep disturbances are potentially modifiable [15–18]. Therefore the successful identification and treatment of sleep problems may have a positive effect on symptoms such as pain, mood and fatigue, resulting in improvements in physical and cognitive functioning and quality of life.

A previous review of sleep disturbances in rheumatological diseases included pSS [19], but this review was published some time ago and the pSS section was predominantly based on one comparative study that used Rheumatoid arthritis (RA) patients as controls. Thus an up-to-date systematic review of the pSS sleep literature, including normative data on healthy controls, is required.

The aim of this review was to identify all the published literature on sleep difficulties in pSS in order to answer the following questions: Are sleep difficulties more prevalent in pSS patients than in the general population and which sleep difficulties are more prevalent in pSS patients than in the general population?

Methods

A systematic review of the published literature on sleep and pSS was conducted. The protocol was published prospectively with PROSPERO, an international prospective register of systematic reviews (CRD42015024977) [20]. The methodological framework used was the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement [21].

Eligibility criteria

Eligible studies were English-language primary research papers published in full. These included intervention, diagnostic, prognostic and aetiological studies with adult participants (>18 years) with a diagnosis of pSS. Case studies and review papers were excluded. Where papers report mixed populations, only studies that analysed the pSS population separately were included. Outcomes had to include sleep outcomes and other outcomes that have a relationship with sleep. In mixed population studies, pSS data had to be reported separately for pSS patients. Data for pSS had to be compared with a control population, which could be healthy controls or controls with other diseases. Therefore studies that did

not compare data from a pSS group with a non-pSS control group were excluded from this review.

Search strategy

Databases [PubMed, Medline (Ovid), Embase (Ovid), PsychINFO (Ovid) and Web of Science] were searched from inception to September 2015 using a prespecified search string (supplementary Table 1, available at *Rheumatology* Online). The references of all included studies were also searched. Two reviewers (K.H. and Z.G.) independently examined the titles and abstracts of all records identified and full papers were retrieved for all papers that met inclusion criteria. All full-text articles were screened by two review authors independently (K.H. and K.D.) for inclusion.

Data extraction and quality assessment

Data were extracted by one author (K.H.) onto a piloted form. These were checked by a second author (K.D.). Risk of bias was assessed at the study level separately by two authors (K.H. and K.D.) using the Joanna Briggs Institute Prevalence Critical Appraisal Tool [22] and specific notes for questions within the tool were agreed upon between the authors (K.H. and K.D.) to reduce ambiguity prior to making a decision for each criteria (supplementary Table 2, available at *Rheumatology* Online). Disagreements between reviewers were resolved through discussion.

Summary measures

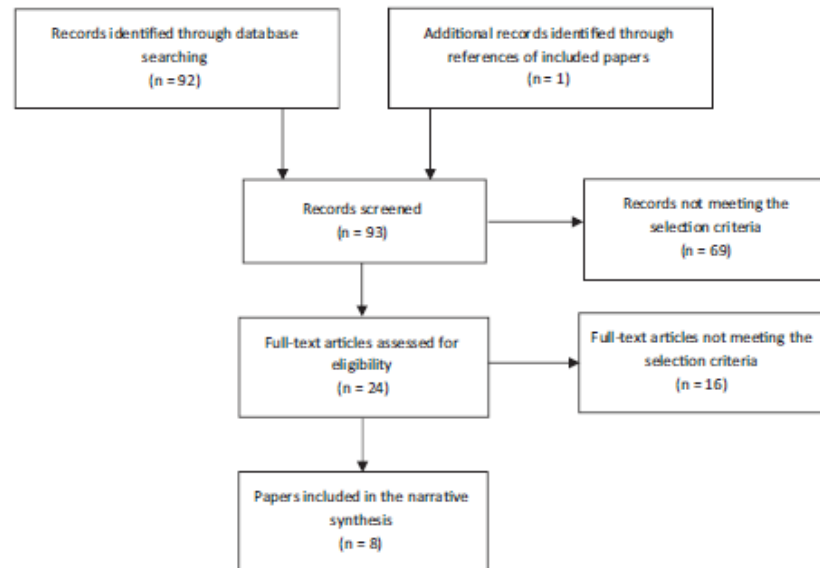
Any sleep summary measure that compared a pSS cohort with a comparative group was extracted. These include differences in means and medians and odds ratios. Data were combined in a narrative synthesis due to the expected heterogeneity of the included studies.

Results

Nine studies from eight publications were identified for inclusion in this narrative review [13, 23–29] (Fig. 1). A summary of the included studies are in Table 1. Sixteen studies did not meet the inclusion criteria. Excluded studies with reasons for exclusion can be found in supplementary Table 3, available at *Rheumatology* Online. One excluded study was a small uncontrolled study ($n = 9$) of a nocturnal humidification device that reduced nocturnal sicca symptoms in the participants [30]. Another excluded study included the use of an artificial saliva water spray, compared with placebo, to improve nocturnal oral dryness symptoms, as improvements were demonstrated in both the placebo and intervention groups [31]. This review did not set out to investigate interventions for pSS sleep disturbances, but these findings are considered in the context of potential future interventions in the discussion.

A total of 93 records were screened. Most studies were excluded at the title stage, as they were not relevant to the review or did not fit the inclusion criteria (Fig. 1). Fourteen publications were examined in more detail before

Fig. 1 Flow diagram of articles included in this review



exclusion (supplementary Table S1, available at *Rheumatology* Online) and nine studies from eight publications were included in this narrative review [13, 23–29] (Table 1). Gudbjörnsson *et al.* [23] included two studies in their paper and these are referred to as Gudbjörnsson *et al.* study 1 (a comparative study of sleep symptoms in three populations) and study 2 (a polysomnography study) in this review for clarity.

Assessment of bias

The risk of bias quality assessment findings of the included studies are presented in Table 2. Three studies included only female pSS participants [13, 24, 29] and were consequently deemed as not being representative of the target population. Two studies (Gudbjörnsson *et al.* studies 1 and 2) [23] used the Copenhagen Classification Criteria [32] to identify their subjects. These criteria are not validated or accepted universally [40], therefore these studies were also scored as not being representative of the target population. The remaining studies [13, 24–29] used either the European Community criteria [41] or the American European Consensus Group criteria [40].

Several studies did not fully specify how their participants were recruited (including Gudbjörnsson *et al.* studies 1 and 2) [13, 23, 24, 28] and uncertainty remained for this item for these studies. The sample size was small (<40) for a number of studies (including

Gudbjörnsson *et al.* study 2) [13, 23, 24, 27, 28] and these studies were scored as being at high risk of bias for this question.

Overall, three studies were deemed to be of high risk of bias (including Gudbjörnsson *et al.* study 2) [13, 23, 24], four at medium risk of bias (including Gudbjörnsson *et al.* study 1) [23, 27–29] and two at low risk of bias [25, 26].

Prevalence of specific sleep difficulties in pSS

The main sleep outcomes are shown in Table 3. Perceived sleep disturbance (measured by sleep diary or patient-reported sleep questionnaires) was reported in four studies (including Gudbjörnsson *et al.* study 1) [13, 23, 26, 28]. Odds ratios (ORs) were calculated from the data provided by one study [26]. pSS patients scored significantly worse than healthy controls for this outcome. It was unclear whether overall there is a higher prevalence of sleep disturbance in pSS patients compared with other disease groups (OA, RA, SLE), as there were inconsistent findings between the studies.

Time spent in bed was assessed in two studies with conflicting findings. One study objectively assessed this outcome with polysomnography (Gudbjörnsson *et al.* study 2 [23]) and the other measured time in bed subjectively with a patient-reported sleep questionnaire [25]. However, the study that reported no difference for this outcome between pSS patients and healthy controls

TABLE 1 Summary of included studies

Author, year and country	Study design	Participants	Sleep outcomes
Goodchild <i>et al.</i> , 2010, UK [13]	Observational prospective study	pSS: <i>n</i> = 14, AECG diagnostic criteria for pSS [29], 100% female, mean age 58 years, MDD 13 years RA: Rheumatoid arthritis <i>n</i> = 25, 100% female, mean age 62 years, MDD 9 years	Sleep diary Actigraphy
Gudbjörnsson <i>et al.</i> , 1993, Sweden [23]	Study 1: cross-sectional sleep questionnaire Study 2: observational study Polysomnography for two consecutive nights	Study 1: pSS: <i>n</i> = 40, Copenhagen diagnostic criteria for pSS [32], 95% female, mean age 53 years. Ten pSS patients also had PSG RA: <i>n</i> = 42, ARA criteria for classical RA: Rheumatoid arthritis [33], 100% female, 10 had symptoms of secondary SS HC: <i>n</i> = 60, 100% female, age matched with the pSS participants Study 2: pSS: <i>n</i> = 10, no demographic information provided HC: <i>n</i> = 30, middle-aged	Study 1: Uppsala Sleep Inventory [34] Study 2: polysomnography
Hilditch <i>et al.</i> , 2008, Australia [24]	Observational study over a night's sleep	pSS: <i>n</i> = 11, AECG diagnostic criteria for pSS, 100% female, mean age 61 years, MDD not reported HC: <i>n</i> = 8, all female, mean age 55.9 years, age matched with patient group	Electroencephalogram, electrooculogram, submental electromyogram; respiratory (inspiratory flow, end-tidal CO ₂ and mask leak); breathing effort; upper airway collapsibility; oral wetness and saliva surface tension
Theander <i>et al.</i> , 2010, Sweden [25]	Cross-sectional survey	pSS: <i>n</i> = 77, AECG criteria for pSS, 90% female, median age 61 years, MDD 12 years HC: <i>n</i> = 59, 90% female, median age 55 years	Epworth Sleepiness Scale [35], Restless Legs Syndrome Questionnaire [36], Lund University Sleep Questionnaire [25], Profile of Fatigue, fatigue VAS
Tishler <i>et al.</i> , 1997, Israel [26]	Cross-sectional survey	pSS: <i>n</i> = 65, AECG classification criteria for pSS, 92% female, mean age 57.3 years, MDD 8.3 years RA (group A): <i>n</i> = 67, 83% female, MDD 12.6 years RA with sicca symptoms (group B): <i>n</i> = 63, 70% female, MDD 15.1 years OA: <i>n</i> = 31, 94% female, MDD 10.3 years	Mini Sleep Questionnaire [26]
Uzmani <i>et al.</i> , 2012, Australia [27]	Observational study	pSS: <i>n</i> = 28, 100% female, AECG classification criteria for pSS, mean age 58.7 years, MDD not stated HC: <i>n</i> = 18, 100% female, mean age 55.8 years	Epworth Sleepiness Scale, polysomnography, Apnoea-Hypopnea Index [27]
van Oers <i>et al.</i> , 2010, Netherlands [28]	Repeated measures study to compare variability of fatigue during the day	pSS: <i>n</i> = 29, 100% female, AECG criteria for pSS, mean age 53.3 years, MDD not stated SLE: <i>n</i> = 23, 100% female RA: <i>n</i> = 19, 100% female HC: <i>n</i> = 52, 100% female, mean age 51 years	15-item Dutch questionnaire on sleep quality [37]
Walker <i>et al.</i> , 2003, Australia [29]	Compared differences in urinary symptoms and daytime sleepiness	pSS: <i>n</i> = 76, European Community criteria for pSS, 100% female, median age 58 years, MDD not stated OA: <i>n</i> = 43, 100% female, median age 64 years	Epworth Sleepiness Scale, FACIT-F [38], American Urological Symptom Index [39]

AECG: American-European Consensus Group Criteria; ARA: American Rheumatism Association; HC: healthy controls; MDD: mean disease duration; OSA: obstructive sleep apnoea; VAS: visual analogue scale.

(Gudbjörnsson *et al.* study 2) [23] had very small numbers and took the measurements in a laboratory. The polysomnography study protocol and environment may have influenced how long a participant remained in bed. Therefore it

is unclear whether pSS patients spend a longer time in bed compared with other populations.

We identified five separate studies that examined total sleep duration, including the Gudbjörnsson *et al.* studies 1

TABLE 2 Assessment of risk of bias

Risk of bias questions	Goodchild <i>et al.</i> , 2010 [13]	Gudbjörnsson <i>et al.</i> , 1993, study 1 [23]	Gudbjörnsson <i>et al.</i> , 1993, study 2 [23]	Hilditch <i>et al.</i> , 2008 [24]	Theander <i>et al.</i> , 2010 [25]	Tishler <i>et al.</i> , 1997 [26]	Usmani <i>et al.</i> , 2012 [27]	Van Oers <i>et al.</i> , 2010 [28]	Walker <i>et al.</i> , 2003 [29]
1. Was the sample representative of the target population?	N	N	N	N	Y	Y	Y	Y	N
2. Were study participants recruited in an appropriate way?	?	?	?	?	Y	Y	Y	?	Y
3. Was the sample size adequate?	N	Y	N	N	Y	Y	N	N	Y
4. Were the study subjects and the setting described in detail?	N	Y	N	N	Y	Y	Y	Y	Y
5. Was the data analysis conducted with sufficient coverage of the identified sample?	?	Y	N	Y	Y	Y	Y	Y	Y
6. Were objective, standard criteria used for the measurement of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y
7. Was the condition measured reliably?	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. Was there appropriate statistical analysis?	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Were all important confounding factors/subgroups/differences identified and accounted for?	Y	?	?	?	Y	Y	?	?	Y
10. Were subpopulations identified using objective criteria?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Adapted with permission from Munn *et al.* [22]. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. *Int J Health Policy Manag* 2014;3:123–8. N: no; N/A: not applicable; Y: yes; ?; unclear.

Table 3 Differences in specific sleep outcomes between pSS patients and controls

Study	Results	pSS
Perceived sleep disturbance	Goodchild et al., 2010 [13] Gudbjörnsson et al., 1993, study 1 [23] Tishler et al., 1997 [26] van Oers et al., 2010 [28] Gudbjörnsson et al., 1993, study 2 [23] Theander et al., 2010 [25] Goodchild et al., 2010 [13] Gudbjörnsson et al., 1993, study 1 [23] Gudbjörnsson et al., 1993, study 2 [23] Hliditch et al., 2008 [24] Usmani et al., 2012 [27] Gudbjörnsson et al., 1993, study 1 [23] Gudbjörnsson et al., 1993, study 2 [23] Usmani et al., 2012 [27] Goodchild et al., 2010 [13] Gudbjörnsson et al., 1993, study 2 [23] Hliditch et al., 2008 [24] Gudbjörnsson et al., 1993, study 1 [23] Gudbjörnsson et al., 1993, study 2 [23] Theander et al., 2010 [25] Usmani et al., 2012 [27] Hliditch et al., 2008 [24] Usmani et al., 2012 [27] Gudbjörnsson et al., 1993, study 1 [23] Theander et al., 2010 [25] Usmani et al., 2012 [27] Walker et al., 2003 [29]	pSS vs RA not significantly different for quality of sleep or feeling of refreshment 44% pSS not feeling rested after sleep vs 9.8% RA ($P < 0.001$) and 15.3% HC ($P < 0.01$) Moderate/severe sleep disturbance 75% pSS. Significantly greater than OA and RA ($P < 0.01$) Significant differences in sleep disturbance ($P < 0.001$) between all groups (SLE, RA, HC, pSS). pSS highest median (6/15), HC lowest (2/3/15). pSS mean time in bed (500 min, range 444–532) similar to HC (range 419–514) pSS 45 min more in bed vs HC (8.24 vs 7.72h; $P = 0.048$) pSS mean 7 h asleep, similar to RA pSS mean of 5.2 h asleep (s.d. 1.90), significantly less than RA (5.8h (s.d. 1.30), $P < 0.05$) and HC (7.2h (s.d. 0.77), $P < 0.0001$) pSS mean 358 min asleep (range 183–473), less than HC range (396–466 min) No difference total sleep time pSS vs HC No difference total sleep time pSS vs HC Mean time to fall asleep greatest in pSS (30 min (s.d. 52.49)) vs RA (21 min (s.d. 19.44)) and HC (19 min (s.d. 6.97)), difference not significant pSS mean 20 min to fall asleep (range 3–65), greater than HC range (1.5–13.6 min) pSS mean 22.8 min to fall asleep (range 14–40) vs 13.8 for HC (range 6–22) ($P = 0.035$) pSS 84% sleep efficiency significantly less than RA 89.4% ($P < 0.05$) pSS 70% mean sleep efficiency, well below control range (84–100%) No difference in pSS group vs HC (combined mean 44% sleep efficiency) pSS woke mean 2.6 times, significantly more than RA (1.5) ($P < 0.0001$) and HC (1.0) ($P < 0.05$) pSS woke mean 19 times (polysomnography) vs HC (range 1–7) pSS awakenings [mean 2.7 (s.d. 0.17)] higher than HC [mean 1.7 (s.d. 0.18), $P = 0.001$] Trend of higher mean nocturnal arousals in pSS vs HC ($P < 0.06$) No difference pSS vs HC ($P = 0.18$) Twice the frequency of apnoea and hypopnoeas in pSS vs HC ($P = 0.032$) Sleep apnoea 64% pSS vs 28% HC ($P = 0.03$) pSS significantly more daytime sleepiness vs HC ($P < 0.001$) or RA ($P < 0.0001$). pSS significantly more daytime naps [pSS 15.2% vs HC 0% ($P < 0.01$), but not RA (21.4%)] pSS significantly worse daytime sleepiness [ESS; mean 9.5 (s.d. 5.2)] vs HC [mean 7 (s.d. 4.0)] ($P = 0.003$) and significantly more excessive sleepiness (15.3%) vs HC (11.9%) ($P = 0.016$) pSS significantly worse for daytime sleepiness [ESS; mean 10.1 (s.d. 5.82)] vs HC [mean 6.5 (s.d. 3.39), $P = 0.014$] pSS daytime sleepiness significantly worse vs OA (OR 2.50, $P = 0.01$)

P-values are reported when provided in the published studies. +, favours controls; ESS: Epworth Sleepiness Scale; HC: healthy controls; ND: no difference.

and 2 [13, 23, 24, 27]. Three small studies [13, 24, 27] compared a total of 53 pSS patients with RA patients ($n=25$) [13] or healthy controls ($n=26$) [24, 27]. They found no significant differences between the groups in terms of total sleep time. However, Gudbjörnsson *et al.* study 1 [23] compared 40 people with pSS with 42 people with RA and 60 healthy controls. They found that people with pSS reported significantly less sleep than the comparators as measured by sleep diaries (40 min–1 h 45 min less), while in their smaller polysomnography study (study 2) they found that pSS patients experienced 1 h 18 min–2 h less sleep than healthy controls.

Three studies examined the proportions of time spent in each of the stages of sleep between pSS patients and controls (including Gudbjörnsson *et al.* study 2) [23, 24, 27]. Two found that pSS patients spent more time in stage 1 sleep than controls (Gudbjörnsson *et al.* study 2) [23, 24]. However, Usmani *et al.* [27] found no such difference. None of the studies found between-group differences for other stages of sleep.

Sleep onset latency (time taken to fall asleep) was not significantly different between pSS patients, RA patients and healthy controls using self-reported methods in one study (Gudbjörnsson *et al.* study 1) [23], although the authors did not make a direct comparison between the pSS and control groups. However, two studies (including Gudbjörnsson *et al.* study 2) [23, 27] involving objective testing of this outcome (polysomnography) did find sleep onset latency to be greater in pSS patients (mean 20–22 min) compared with controls (mean 13.8 [27], range 1.5–13.6 min [23]).

Sleep efficiency (percentage of time spent in bed asleep) was identified as reduced in people with pSS in two studies (including Gudbjörnsson *et al.* study 2) [13, 23], both of which used objective measures. In a third study [24] with very low numbers, the sleep efficiency was very poor for both groups. However, this could be due to the nasal mask that participants wore and the regular negative pressure pulses used to measure airway collapsibility, which may have interfered with their sleep. Thus the environment was not ideal to examine sleep efficiency in this study.

All studies that examined the number of night awakenings found that these were increased in pSS patients (Gudbjörnsson *et al.* study 2 and Theander *et al.*) [23, 25] (see Table 3). That being said, the polysomnography studies that report an arousal index (number of times sleep is interrupted) found no difference between pSS patients and comparison groups [24, 27].

Factors associated with disturbed sleep

A number of studies examined specific reasons for waking in the night. Theander *et al.* [25] noted that 13% of their pSS group reported sicca symptoms that disturbed their sleep, compared with none of their controls.

Hilditch *et al.* [24] found that nocturnal oral dryness did not differ significantly between pSS patients and controls, which is surprising, but due to their very low numbers, could be a type II error. The same authors found that

saliva surface tension showed no difference between the groups in the early morning but was significantly higher in the pSS group in the late evening.

Nocturnal pain and disturbed sleep was more common in pSS compared with controls and RA patients (Gudbjörnsson *et al.* study 1 and Theander *et al.*) [23, 25]. Gudbjörnsson *et al.* study 1 [23] reported that 54% of their pSS group experienced nocturnal pain compared with 37% of their RA group ($P<0.01$) and 0% of their healthy control group ($P<0.0001$). Theander *et al.* [25] found that nocturnal pain that disturbed sleep was present in 19% of their pSS group, which was >9% of those in the control group, although this difference was not significant ($P=0.07$).

There was conflicting evidence from two studies for nocturia disturbing sleep in pSS patients. Walker *et al.* [29] investigated nocturia and found no difference between pSS patients and an OA population for the occurrence of this symptom (OR 0.93, $P=0.85$). Conversely, Theander *et al.* [25] found that 53% of their pSS participants experienced nocturia that disturbed sleep compared with 26% of their healthy controls ($P=0.001$).

Autonomic symptoms

Nocturnal autonomic symptoms were only investigated by Gudbjörnsson *et al.* study 1 [23], which found 20% of the pSS participants in this study reported experiencing nocturnal sweating, which was greater than their RA comparison group (12%, NS) and their healthy controls (2%, $P<0.01$). Palpitations at night were reported in 5% of their pSS group, which were not present in either their RA or healthy control groups.

Presence of co-morbid sleep disorders

In Theander *et al.*'s study [25], 2 of their 72 patient pSS cohort self-reported a diagnosis of narcolepsy, compared with none of their controls, but this was not reported as an outcome in any of the other included studies.

Using polysomnography, one study noted the occurrence of obstructive apnoeas and hypopnoeas were double in their pSS group compared with healthy controls [27]. In this study, continuous positive airway pressure (CPAP) treatment was offered to 8 of 28 pSS study participants who were identified as having severe sleep apnoea (with an apnoea-hypnoea index score ≥ 40). Five participants accepted the treatment and significant improvements were demonstrated both in their Epworth Sleepiness Scale (ESS) scores and fatigue scores at 2–6 months after commencing CPAP treatment.

However, another study [24] investigated upper airway collapsibility and found no difference in both the upper airway collapsibility index and a range of respiratory variables between their pSS and control groups, but this could be due to the study being underpowered.

Daytime somnolence

Four studies identified increased daytime sleepiness in patients with pSS compared with healthy controls.

Gudbjörnsson *et al.* study 1 [23] found their pSS patients were sleepy in the daytime five times more frequently than RA controls and almost three times more frequently than healthy controls. Theander *et al.* [25], Usmani *et al.* [27] and Walker *et al.* [29] reported that ESS scores were significantly higher in pSS patients than in controls.

Discussion

Findings of the review

We have found that subjective and objective sleep disturbances are more common in pSS patients. Further research is needed to examine the differences between pSS patients and other disease groups.

There were inconclusive findings regarding whether pSS patients spend more time in bed than comparative groups, however, if they do spend longer in bed, it is likely that this is due to the sleep disturbances and night awakenings they experience. Because of the conflicting findings in this review, further studies are needed to confirm whether pSS patients have a short sleep duration compared with other groups. However, pSS patients do seem to experience more frequent nocturnal awakenings than other groups. Despite this finding, the arousal index scores were not found to be greater for pSS patients in the studies that examined this outcome. One reason could be due to low numbers of participants in these studies. However, an alternative suggestion is that the pSS patients awaken more frequently during these arousals due to their symptoms, such as dryness, pain and autonomic symptoms. A further possibility is that pSS patients may demonstrate high-frequency electroencephalographic activity throughout the night that may influence their perception of sleep and wakefulness. Further investigations are required to test this.

Sicca symptoms did disturb sleep in one study [25] and potential interventions to reduce these symptoms and thus improve sleep will be discussed shortly. Pain is another symptom that is more common in pSS patients during the night. Segal *et al.* [4] observed that sleep quality is reduced as pain increases. Thus if pain is reduced, sleep quality may improve.

There were conflicting findings regarding the symptom of nocturia in pSS patients. Since pSS patients regularly drink to ease the symptoms of their dryness, needing the toilet during the night could be a natural consequence of this.

Although autonomic symptoms were only reported in one included study, there is a greater prevalence of these symptoms in pSS patients [3] and it is logical that these symptoms, which can include palpitations, dizziness and sweats, may interfere with sleep.

There does seem to be an increased prevalence of obstructive sleep apnoea in pSS patients, although further studies are needed to reproduce this finding. The ESS can be used as a screening tool to identify patients who are at risk of obstructive sleep apnoea [42] and these patients should be referred for further investigations.

This review has demonstrated that daytime sleepiness is a problem in pSS patients. Daytime sleepiness correlates with reduced quality of life [10], fatigue [25, 29], autonomic dysfunction [3] and functional impairment [6]. Furthermore, patients who are functionally impaired have significantly greater ESS scores than those who experience no functional disability [6].

Potential interventions for sleep disturbances in pSS

Interventions that address the perception of poor sleep without the necessity for objective verification include addressing unhelpful beliefs surrounding sleep, addressing sleep efficiency and prescribing time in bed. These are all components of a Cognitive Behavioural Therapy for Insomnia (CBT-I) intervention [43]. CBT-I is considered a first-line treatment for insomnia associated with a medical condition [44] and is an effective intervention in other long-term conditions [45], therefore it could be beneficial in pSS. Time in bed and sleep efficiency are both addressed in the sleep restriction component of a CBT-I intervention and this may be a useful way of addressing longer time spent in bed awake in this patient group and lead to improved sleep. Further studies of CBT-I and various modes of delivering this intervention are therefore warranted in this patient group.

Nocturnal humidification and artificial saliva sprays may ease nocturnal sicca symptoms and decrease sleep disturbances in pSS patients and are unlikely to contribute to bladder disturbances during the night. Although a humidification device did seem to be a promising intervention in an excluded study [30], further appropriately powered studies comparing nocturnal humidification devices in pSS with controls are required to demonstrate efficacy.

For autonomic symptoms that interfere with sleep, appropriate interventions addressing these symptoms, such as water bolus treatment during the day [46], may also help to improve sleep, particularly if these symptoms are regularly experienced during the night. Further research is required to demonstrate the efficacy of interventions for dysautonomia in pSS, such as blood pressure dysregulation, on sleep outcomes.

Further considerations

A more detailed sleep assessment, including polysomnography, may be beneficial for this group when considering the level of sleep apnoea reported in this population. Moreover, polysomnography will afford a closer examination of other objectively verifiable sleep disorders that may influence sleep (e.g. narcolepsy, periodic limb movement disorder, restless legs syndrome and hypersomnolence disorders). If severe sleep apnoea is identified in pSS patients, CPAP treatment should be offered [47].

Pain is another symptom that can interrupt sleep. pSS patients who experience pain that is interfering with their sleep should be offered appropriate pain management interventions [4]. CBT-I is efficacious in improving sleep duration, continuity and perceived quality in chronic pain

patients with co-morbid insomnia and CBT-I with an additional pain component is feasible [45]. A pain adjunct to a CBT-I intervention may therefore improve sleep in pSS patients with chronic pain. Interventions targeting sleep disturbances in pSS may improve daytime sleepiness and fatigue, which could result in increased functional capacity and quality of life.

There are some limitations to this review. First, although we did not specifically investigate potential causes of sleep disturbances, we uncovered several potential contributing factors from within the included studies. However, there may be further potential complications in pSS that might play a role in sleep disturbance, such as gastro-oesophageal reflux [48]. Further work needs to be done to determine the causes of sleep disturbances in this patient group. Second, although we did not set out to investigate specific interventions for sleep disturbances, we identified some uncontrolled studies of interventions for sleep in pSS. There may therefore be further studies of interventions for sleep disturbances in pSS uncovered by our search. However, a recent systematic review of all non-pharmacological interventions for pSS did not identify any randomized controlled trials for sleep difficulties in this patient group [49]. Furthermore, recent meta-analysis of 23 studies determined that CBT-I was efficacious in reducing sleep disturbances and improving sleep quality in patients with insomnia secondary to a co-morbid condition [50].

This review included a total of 350 pSS patients in nine separate studies. Only two studies (with 142 pSS patients) were deemed to be at low risk of bias. This highlights the paucity of high-quality research into sleep disturbances in pSS patients.

Conclusion

From the included studies in this review, we found an increased prevalence of sleep disturbances in pSS patients compared with controls, including daytime somnolence, subjective sleep disturbances (including disturbance due to dryness symptoms) and increased occurrence of night awakenings. Sleep apnoea may be more common, but further polysomnography studies are required to confirm this.

Although we did not set out to investigate interventions, logic dictates that CBT-I for sleep disturbances and night awakenings and nocturnal humidifiers for nocturnal sicca symptoms would be beneficial in this patient group. However, further studies are required to confirm their effectiveness in pSS. Due to the variable quality of the included studies, the mix of outcomes assessed within these studies and the overall low numbers of patients included within them, we recommend further studies to add to the body of pSS sleep prevalence literature. Finally, in the presence of sleep difficulties in pSS patients, primary sleep disorders should be screened for and treated appropriately.

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Supplementary data

Supplementary data are available at *Rheumatology Online*.

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A concept mapping study evaluating the UK's first NHS generic fatigue clinic

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Abstract

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Importance Fatigue is a significant and debilitating symptom affecting 25% of the population. It occurs in those with a range of chronic diseases, can be idiopathic and in 0.2–0.4% of the UK population occurs in combination with other symptoms that together constitute chronic fatigue syndrome (CFS). Until recently, NHS clinical services only focussed upon CFS and excluded the majority of fatigued patients who did not meet the CFS diagnostic criteria. The CRESTA Fatigue interdisciplinary clinic was established in 2013 in response to this unmet need.

Objective To identify the service needs of the heterogeneous group of patients accessing the CRESTA Fatigue Clinic, to prioritize these needs, to determine whether each is being met and to plan targeted service enhancements.

Design Using a group concept mapping approach, we objectively identified the shared understanding of service users accessing this novel clinic.

Setting NHS Clinics for Research & Service in Themed Assessment (CRESTA) Fatigue Clinic, Newcastle Upon Tyne, UK.

Participants Patients ($n = 30$) and referrers ($n = 10$) to the CRESTA Fatigue Clinic contributed towards a statement generation exercise to identify ways the clinic could support service users to improve their quality of life. Patients ($n = 46$) participated in the sorting and rating task where resulting statements were sorted into groups similar in meaning and rated for 'importance' and 'current success'.

health-care systems.¹¹ Subsequently, the Clinics for Research & Service in Themed Assessment (CRESTA) Fatigue Clinic was established to address this service gap with the implicit aim of meeting the needs of patients with chronic fatigue, irrespective of their physical health diagnosis. It is based on a Dutch model.¹² The CRESTA Fatigue Clinic is an interdisciplinary clinic with occupational therapy, physiotherapy, sleep therapy, health psychology, nursing and medicine. To our knowledge, it is the first of its kind in the UK NHS. Consequently, demand for the service is high, with patients travelling long distances to be seen. Although patients accessing the service are offered therapy if appropriate, it remains unclear whether the service offered is meeting their expectations or requirements, without involving them fully in a comprehensive planning and evaluation project. This is vital to determine both the importance of individual expectations and the success of whether these expectations are being met.

The objectives of the service evaluation were to identify the service needs of the heterogeneous group of patients accessing the clinic, to prioritize these needs, to determine whether each need is being met and then to plan targeted service-user-informed service enhancements.

Methods

Group concept mapping methodology (GCM), developed by Trochim,¹³ is a mixed-methods participatory approach which uses a combination of group processes (brainstorming, sorting, rating and interpretation) and a sequence of multivariate statistical analysis steps (multidimensional scaling and hierarchical cluster analysis) that result in concept maps. Concept maps are visual representations of how participants conceptualize the relationship between ideas which they have generated on a particular topic. Priority values are added by participants to qualitative statements gathered during the brainstorming phase, and these can be interpreted in pattern matches and value plots and used in planning or evaluation studies.¹⁴

Group concept mapping typically involves five distinct phases:

1. Ideas generation/brainstorming

Participants who have a common area of interest are asked to provide their opinion in response to a focus prompt. Typically, a focus prompt is an incomplete sentence which stakeholders complete as many times as they like. This results in a list of ideas/statements.

2. Statement reduction

Duplicate statements are removed, and the refined statement list is checked for syntax and readability by the research team.

3. Sorting activity

Each statement is numbered and printed onto an individual card. Participants are asked to sort all the statements into piles of similar meaning statements and to give each pile a name. Participants record on a sheet the name of each pile they have created and statement numbers of the cards they contain.

4. Rating activity

Participants are given a list of the numbered statements and are asked to give each statement a value judgement (such as 'importance') on a 1–5 Likert scale.

5. Data analysis

The sorted data from each participant are entered into a software package specifically designed for GCM projects (Concept Systems Global Max™). Through a mathematical process of multidimensional scaling and hierarchical cluster analysis, concept maps are generated. Statements are represented by numbered points on the map. Statements that have been sorted together (often by participants) will be close together on the map and will be similar in meaning. Statements that are infrequently sorted together by participants will be located further from each other on the map and will be less similar in meaning. The cluster analysis results in clusters on the map which contain similar meaning statements and represent how the group see the ideas which they have generated. The software suggests names for the clusters based on the names participants gave to their piles in the sorting exercise.

The rating data are then analysed and used to produce 'pattern matches' and 'go-zones'. Pattern matches represent the value judgement for the rating scales for each of the generated cluster themes. Go-zones are bivariate value plots which can be used to prioritize the statements. Both pattern matches and go-zones can be used to evaluate and prioritize the clusters/themes and individual statements within them.

A strength of GCM over other approaches is that it is considered to be an equitable process, giving an equal voice to all participants, does not direct them to form a consensus and can be conducted with relatively large numbers of people representing different stakeholder groups. GCM offers an alternative approach to traditional open-ended service evaluation questionnaires or face-to-face interviews. These require word-analysis approaches and forced category classifications which inherently will have some level of researcher bias.¹⁵ In GCM, the statement data are classified into themes or clusters using a mathematical process which incorporates each participants' sorting data equally and can be used to observe the combined value judgements of all participants. GCM uses a structured mixed-methods approach to capture ideas from an identified group.¹⁶

GCM has been used in a variety of health-care settings to plan, evaluate and make improvements to existing policy, interventions and services. This includes public health^{17–20} rheumatology,^{21,22} mental health,^{23,24} cancer care²⁵ and rehabilitation.²⁶

This project was reviewed by the Research and Governance Department and was considered to be a service evaluation, meaning no research ethics committee permissions were required. The evaluation was registered as a service audit with the Newcastle upon Tyne Hospitals NHS Foundation Trust.

The participants

Participants were identified in two distinct parts of the GCM process: during the ideas-generation phase and again during the sorting

and rating activities. First, all physicians ($n = 55$) who had referred patients to the CRESTA Fatigue Clinic received the brainstorming exercise by post. No identifiable patient information was provided. This was completed by 10 general practitioners and hospital consultants. Consecutive patients attending the CRESTA Fatigue Clinic took part in the anonymous brainstorming activity during their usual clinic attendance. The activity was made available in 12 consecutive clinics for patients to complete and place in a box in the waiting area. This was completed by 30 participants.

Secondly, the sorting and rating activities were posted out to 147 patients who had attended at least one appointment at the CRESTA Fatigue Clinic over its first year. Forty-six took part in the sorting and/or rating tasks giving a return rate of 32%.

To develop a formal action plan, the final results were reviewed in consultation with a trained group of Health Champions who were ex-patients specifically recruited from the CRESTA Fatigue Clinic in a project undertaken in collaboration with NHS England North and Altogether Better.²⁷ Our Health Champions are a team of ex-patients who have been brought together by a team from NHS England North, trained and empowered to feedback regarding their own and others' experiences of attending the clinic and to develop their own strategies to enhance the clinic experience.

Data collection

Generation of ideas (brainstorming)

In the first stage of the study, we asked referrers and clinic patients to complete the following sentence as many times as they could on a piece of paper:

A specific way the CRESTA Fatigue Clinic could support me to improve my quality of life is...

The resulting statement set was reduced to a shorter list of unique ideas¹⁴ with each statement coded with a keyword. Groups of statements containing the same keyword were considered in turn by the authors. Duplicate ideas were

removed, statements that described the same or overlapping ideas were combined, and the resulting statement list was edited for syntax, and to ensure it would be easily understood. For example, 'Making it possible to discuss symptoms as they arise if GP can't find anything wrong' was rephrased to 'an opportunity to discuss my symptoms'. This process resulted in a synthesized statement list of 78 unique ideas (Table S1).

Structuring the ideas: rating and sorting

The refined statement set was mailed to 147 patients. They were asked to rate each statement on two dimensions – (i) *IMPORTANCE* and (ii) *CURRENT SUCCESS* on 1–5 rating scales. The instructions for the importance rating were 'rate each statement below on how IMPORTANT you think it is by putting a circle around a number'. The number 1 on the rating scale represented 'relatively unimportant' and 5 'extremely important'. The current success rating instructions were 'rate each item according to how successful the CRESTA Fatigue Clinic is at addressing that need currently', and 1 on the scale represented 'Need not being met at all' and 5 'Need is successfully met'.

These patients were also given the option of completing a sorting task. The recommended number required for the sorting activity is 25.¹⁶ Because this task is time-consuming, we expressed this activity was optional. Each statement was given a number and printed on a separate card. Participants were asked to sort the cards into groups that they felt were similar in meaning. Participants were then instructed to give each group of statements a name and to document them on a recording sheet with the corresponding statement numbers.

Analysing the data

The analyses were performed using Concept Systems Global Max™ software, specifically designed for GCM projects. Firstly, multidimensional scaling techniques were performed on the card sorting data, which had been arranged into a similarity matrix to position each statement in relation to each other as a

point on an x–y axis. This generated a point map with each point representing a statement. The stress value, a statistic that reflects stability within the overall map, was generated. Instability in the point locations within the map occurs as the location of the points is calculated in multiple dimensions and is being confined to two-dimensional space for easy visual representation. Ideal stress values for concept mapping analyses are below 0.36.¹³ Secondly, hierarchical cluster analysis was performed using Ward's algorithm which created clusters of statements. The clusters were examined by the authors, and maps containing as many as 16 clusters and as few as 4 were examined in an initial interpretation session in a process described by Kane and Trochim.¹⁴ In this process, the software was utilized to combine clusters one at a time by the authors. The statements within each cluster were examined to ensure they conveyed an overall theme. This is a qualitative decision made when it no longer makes sense to proceed to the next iteration as the contents of the cluster would be conceptually too broad. A provisional cluster solution was decided upon by the authors through discussion and agreed upon by our group of Health Champions.

Next, the rating data were considered. Importance and current success ratings were examined both at cluster level in a pattern match and at statement level in a go-zone. The pattern match evaluated both importance and success of the themed clusters. The go-zone allows the statements to be compared in a bivariate plot with mean rating scores for both importance and current success as cut-offs to highlight zones. Statements falling above the mean cut-off score received above-average scores by participants, and those that fall below the mean cut-off score received below-average scores. The zones of particular interest were high importance and high current success (priority needs that are being successfully met) and high priority and lower current success (priority targets for service enhancement). The individual priority targets for service enhancements have been addressed by teams of service-user Health Champions and clinic staff.

Results

Ten referrers and 30 individuals attending the CRESTA Fatigue Clinic completed the brainstorming exercise, generating 154 statements that were subsequently distilled to a final statement set of 78. As the brainstorming was anonymous, we do not have participants' demographic information. Forty-six participants took part in stage two (sorting and rating). The mean age was 62.25 (SD 10.83). Of the 46 participants, 31 completed the sorting task, 46 completed the importance rating, and 40 completed the current success rating. Six participants opted not to complete the current success rating as they had only attended the clinic once and did not feel able to comment.

Concept maps

Multidimensional scaling resulted in a point map with a stress value of 0.24. An eight-cluster solution was agreed upon the following: (i) *clinic purpose*; (ii) *support to self-manage*; (iii) *peer support*; (iv) *lifestyle advice and support*; (v) *access to allied health services*; (vi) *communication*; (vii) *telecare*; and (viii) *service operation*. The smallest cluster (Telecare) contained three statements and the largest (Support to self-manage) 18 statements. The point cluster map can be seen in Fig. 1. Here, each statement is represented by a numbered point on the map (individual statements can be viewed in Table S1). The points are grouped into the named clusters:

Clinic Purpose: The statements within this cluster represent the key purpose for the clinic. Typical statements within this cluster include '#8 – Take my fatigue seriously', '#1 – Improve my health', '#71 – Look at my symptoms as a whole' and '#18 – Deliver a personalised treatment programme' and '#63 – Being offered a physical assessment'.

Support to self-manage: This is the largest cluster containing 18 statements. These include accessing support from a multidisciplinary team of health professionals who have expertise in fatigue (e.g. '#40 – Provide access to a dedicated team of professionals (medical, cognitive behavioural therapy, occupational therapy and physiotherapy) with expertise and an interest in fatigue'). Other statements within this cluster relate to support to manage specific symptoms such as dizziness (#55), pain (#61) and anxiety (#77) as well as support to make behavioural changes to increase activity/exercise levels (#68) and on balancing daily activities and rest (#66).

Peer support: Statements within this cluster relate to support patients could potentially give and receive from each other and include the following statements: '#4 – Make it possible for me to be in touch with others who have fatigue' and '#25 – Meet other people with similar problems and learn how they manage'.

Lifestyle advice and support: Statements such as '#6 – Support with managing work and/or

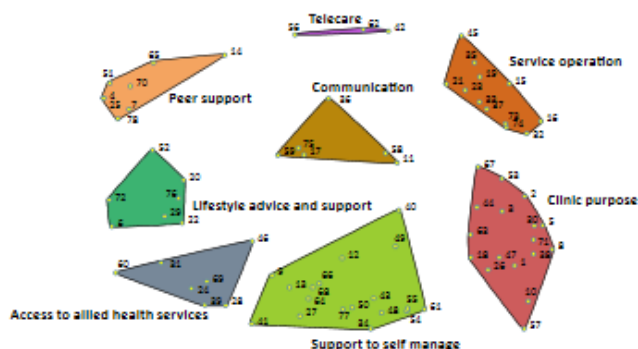


Figure 1 An eight-cluster map showing the distribution of the individual statements as numbered points.

education' and '#72 – Advice about financial support' were representative of statements within this cluster.

Access to allied health services: This cluster included statements regarding accessing non-medical health-care professionals including occupational therapy (#46), physiotherapy (#24) and psychological support (#31 and #69) and access to specialist exercise programmes (#39, #28 and #60).

Communication: This cluster is at the centre of the concept map, indicating its central theme. The central location indicates that the clusters' statements will have regularly been sorted with other statements within all surrounding clusters, despite it being a unique cluster. Statements include '#11 – Provide a culture of understanding which leaves patients understood and less isolated' and more concrete forms of communication such as providing written information about fatigue and interventions (#58) and letters in support of adjustments within the workplace (#36) and benefits claims (#59).

Telecare: This is the smallest cluster and contains only three statements all relating to remote clinic access, including by telephone (#42), by Skype or similar (#62) and online drop in clinics (#56).

Service operation: This cluster contains statements about how the clinic is run including appointments (#74, #32 and #35), training

medical students within the clinic about fatigue for future doctors (#19) and offering opportunities for clinic patients to participate in research projects (#21).

Comparisons between importance and current success ratings of the themed clusters can be seen in a 'pattern match' (Fig. 2). The correlation between ratings was high ($r = 0.91$). A 'go-zone' bivariate plot was created which demonstrates the importance of each individual statement and whether it is being successfully met or not (Fig. 3). Important needs that are being met fall within the green quadrant of the go-zone (Table 1). Important needs that are not being met falling within the yellow quadrant of the go-zone are service enhancement targets (Table 2).

Discussion

This novel service is successfully meeting the majority of important needs and has highlighted some specific targets for service enhancement. Only a small number of priority needs were not being successfully met. Most targets are being addressed by clinic staff in consultation with Health Champions, with the exception of '#57 – cure my problem' deemed not realistically achievable.

This study has highlighted that the novel service being delivered in the Newcastle CRESTA addresses a considerable unmet need. A recent

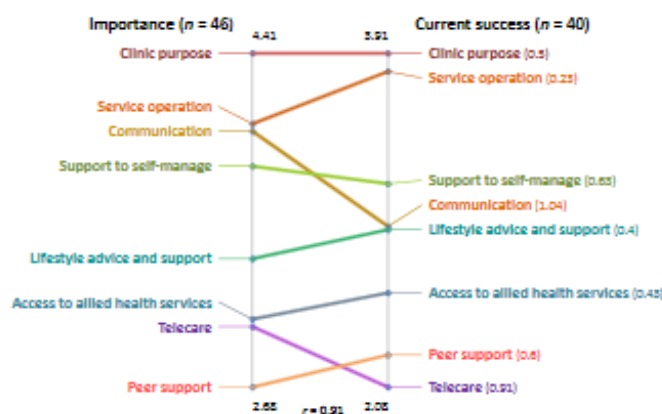


Figure 2 Pattern match demonstrating rating results at cluster level. Mean scores for statements falling within each cluster are demonstrated and clusters that were given comparatively higher scores are positioned nearer the top of the pattern match.

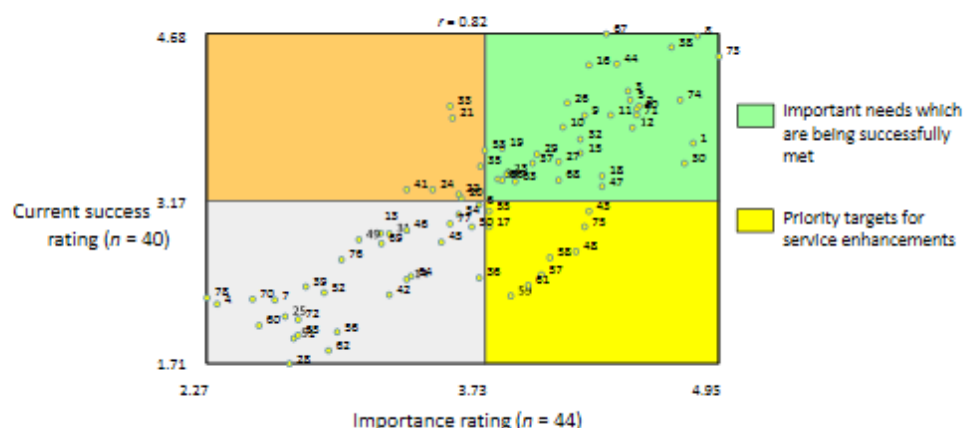


Figure 3 Go-zone of all statements demonstrating rating results for each individual statement. Important needs that are being successfully met. Priority targets for service enhancements.

audit of our CFS NHS Clinical Service confirmed that 40% of those referred with a presumed diagnosis of CFS did not meet the diagnostic criteria for this condition but had fatigue related to other conditions.⁶ In addition, there is considerable recognition that the increase in chronic disease is likely to have a significant burden upon health-care utilization in the coming decades. Simply managing the chronic disease does not necessarily impact upon the symptoms experienced by those affected. Developing strategies that address specifically the symptoms experienced by individuals (such as fatigue) are vitally important, if the true benefits of chronic disease management are to be realized. In addition, NHS CFS/ME clinical services and the NICE guidelines²⁸ do not recommend that individuals with CFS who experience symptoms such as postural dizziness or loss of consciousness (known to occur in almost 90% of CFS patients²⁹) have specific testing for dysautonomia.

This study created a large number of statements suggesting considerable expectations of individuals attending the service. Their expectations were diverse and heterogeneous, underlying the necessity for a multidisciplinary approach to symptom management. The themed clusters cut across a range of areas and highlight

the complexity of symptom and chronic disease management. It is vital that as chronic disease prevalence increases, the UK NHS develops models of care that are able to meet patients' needs and address these complex issues.

The study confirms that the clinic model (despite being early in its conception and implementation) is addressing a large number of areas for this patient group. The statements rated highest and the most successful suggest that fatigue patients value the outpatient attendance. Some statements suggest that experiences in other clinical services may have been suboptimal (e.g. #8, 'Take my fatigue seriously'; #38, 'Believing my symptoms'; #10, 'Give me hope'; #53, 'Time in appointments to express my feelings'; #11, 'Provide a culture of understanding which leaves patients understood and less isolated'). This is disappointing. Recognizing that these symptoms can be extremely debilitating and impact dramatically upon quality of life highlights the need to incorporate symptom management into current systems.

The holistic, multidisciplinary approach that is central to the CRESTA Fatigue Clinic in Newcastle is valued by the patient group (#40, 'Provide access to a dedicated team of professionals (medical, cognitive behavioural therapy, occupational therapy and physiotherapy) with

Table 1 Important statements/needs that were met successfully by the CRESTA Fatigue Clinic

Statement number	Statement	Mean current success rating (1–5)
67	Face to face contact	4.69
8	Take my fatigue seriously	4.68
38	Believing my symptoms	4.58
73	Keep the clinic going	4.50
44	An opportunity to discuss my symptoms	4.44
16	Copy of letters to GPs to be sent to patients	4.43
3	Provide up to date advice	4.21
74	Offer follow up appointments	4.13
26	Help me to understand my symptoms	4.08
5	Provide me with a diagnosis	4.08
2	Inform me of my test results	4.08
40	Provide access to a dedicated team of professionals (medical, cognitive behavioural therapy, occupational therapy and physiotherapy) with expertise and an interest in fatigue	4.00
11	Provide a culture of understanding which leaves patients understood and less isolated	3.97
71	Look at all my symptoms as a whole	3.97
9	Inform me how I could make beneficial changes to some of my behaviours	3.97
10	Give me hope	3.85
12	Support me to better manage my symptoms	3.84
32	Appointments to review my progress periodically	3.77
1	Improve my health	3.71
19	Have medical students in clinic so they can learn about fatigue	3.69
15	Co-ordinate appointments with different members of the clinic team on the same day	3.68
29	Provide support, encouragement and reassurance	3.64

Table 1. Continued

Statement number	Statement	Mean current success rating (1–5)
37	Clinic staff to liaise with other clinicians and agencies (when appropriate)	3.59
27	Support me to manage my daily activities	3.57
30	Investigate potential causes of my fatigue and offer treatments for them	3.51
18	Deliver a personalised treatment programme	3.49
23	Provide information to referring doctors about the clinic and the referral criteria	3.42
63	Being offered a physical assessment	3.38
34	Assist me in reaching my unique goals	3.35
66	Advice on balancing activities and rest	3.35
68	Advice on how to increase activity/exercise levels without reaching burn-out	3.35
47	Help to distinguish which symptoms are due to which condition	3.34

Statements rated high for both importance and current success scores are demonstrated.

expertise and an interest in fatigue'), and one of the high importance/priority statements is the need for continued intermittent follow-up (#74, 'Offer follow up appointments').

The sense of being cast free from an outpatient clinic for those with chronic disease can be extremely isolating. In the clinic, we are now working with our Health Champions to develop strategies that will fulfil some of the needs of this patient group beyond the immediacy of the clinical service. It is arguable that much of what this patient group require should be met in primary care. Currently, this appears not to be the case and there is a real need to develop clinical services that bridge between primary and secondary care for patients with chronic disease who have on-going debilitating symptoms.

Table 2 Important statements/needs that were not successfully met and are targets for service enhancements

Statement number	Statement	Mean current success rating (1–5)
59	Provide letters giving information on my health and abilities for benefit claims	2.36
61	Help to manage pain	2.49
57	Cure my problem	2.51
48	Help me cope with brain fog	2.73
58	Provide written information about my condition, available treatments and other helpful services	2.76
17	Help me to explain my symptoms to others to help them to better understand	3.00
75	Keep me informed of new research findings	3.05
55	Help me overcome my dizziness	3.08
43	Provide new ways to help me cope with the fatigue	3.11

Statements rated high for importance and low for current success are demonstrated.

Clearly, the current NHS model of 'ologies' and the immediacy of 'new to review' ratios do not fit cleanly with the model that is desired by this patient group. If we are to avoid the revolving door element of chronic disease patient management, it is essential that different models of care are evaluated and implemented in order to meet the needs of this increasing patient group.

There are some needs patients feel the clinic does not meet. We, alongside Health Champions, are addressing these. Specifically for statements #59 and #58, we have developed generic fatigue information for patients attending the clinic, something which has not previously been available; for #61 and #48, we are increasing the information available regarding pain and the symptom of brain fog to aid self-management; and for #75, #55 and #43, we have a very active research programme in Newcastle with the Newcastle Fatigue Research Centre. The patients who are seen in the clinic directly link into any on-going research studies,

and the results of these studies are disseminated back to those attending the clinic. This is clearly something that this patient group value enormously.

It is important to acknowledge some potential limitations of this study. This study began when the clinic was in its infancy. Because all patients who had accessed the service were invited to take part, they may have attended the clinic before there was a full complement of therapy staff. This may have affected the results. Despite this, there are only a small number of priority needs that were not being successfully met. Although one is not realistically achievable at this moment in time (#57, Cure my problem), the other targets are currently being addressed by clinic staff in partnership with our service-user Health Champions who are acting as advocates for the patients attending the clinic and developing a peer support system.

The average age of respondents in this service review was 62.25; this is considerably older than that in CFS/ME-specific clinics (males: 41.4, females: 38.6).³⁰ As a result, their service needs may be different to younger patients. As the UK population ages, the demand for such clinics is likely to increase.

Concept mapping is a relatively recently developed methodology. It has some advantages in that it is considered to be an equitable process, giving an equal voice to all participants and does not direct them to form a consensus as in other methods such as Delphi. Once the data has been collected and inputted into the software, the quantitative analyses can be conducted often using a large sample size, relatively quickly prior to being presented to stakeholders for discussion and interpretation. It offers an alternative, systematic approach to traditional open-ended service evaluation questionnaires or face-to-face interviews. A disadvantage is that it requires specialist training and a software licence which can be costly, depending on the size of the project. In the future, concept mapping could be used to track service changes and to facilitate co-design of new services.

The return rate for the questionnaires was 32%; consequently, we must accept that the

needs discussed may not be fully representative of all CRESTA patients. However, the required number for statistical analysis was exceeded.¹⁶

Overall, the UK's first NHS generic interdisciplinary fatigue clinic is a success. It provides patients with the access to a multidisciplinary approach who would otherwise not receive this level of care. The service users value the clinic and are keen for it to be continued. They have highlighted some specific areas for service enhancements which will tailor the service further to the needs of the patients.

Authors' contributions

KH developed the concept and designed the study. It was conducted by KH and RL. All authors contributed to the analysis of the data. JN supervised the project, and the manuscript was written and commented on by KH, JN and RL.

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Conflict of interest

None declared.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Mean priority ratings of all participants.

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Original article

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A systematic review of non-pharmacological interventions for primary Sjögren's syndrome

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Abstract

Objective. To evaluate the effects of non-pharmacological interventions for primary SS (pSS) on outcomes falling within the World Health Organization International Classification of Functioning Disability and Health domains.

Methods. We searched the following databases from inception to September 2014: Cochrane Database of Systematic Reviews; Medline; Embase; PsychINFO; CINAHL; and clinical trials registers. We included randomized controlled trials of any non-pharmacological intervention. Two authors independently reviewed titles and abstracts against the inclusion/exclusion criteria and independently assessed trial quality and extracted data.

Results. A total of 1463 studies were identified, from which 17 full text articles were screened and 5 studies were included in the review; a total of 130 participants were randomized. The included studies investigated the effectiveness of an oral lubricating device for dry mouth, acupuncture for dry mouth, lacrimal punctum plugs for dry eyes and psychodynamic group therapy for coping with symptoms. Overall, the studies were of low quality and at high risk of bias. Although one study showed punctum plugs to improve dry eyes, the sample size was relatively small.

Conclusion. Further high-quality studies to evaluate non-pharmacological interventions for PSS are needed.

Key words: Sjögren's syndrome, systematic review, non-pharmacological, interventions, rheumatology, fatigue, dryness, pain, function.

Rheumatology key messages

- This is the first published systematic review of non-pharmacological interventions for primary SS.
- We identified no evidence to support any non-pharmacological interventions to improve primary SS.
- Further quality, appropriately powered randomized controlled trials of non-pharmacological interventions for primary SS are required.

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Introduction

Primary SS (pSS) is a systemic autoimmune disease primarily affecting exocrine glands, resulting in dry eyes and dry mouth [1]. It has a female preponderance [2], and a recent meta-analysis has identified a prevalence rate of 74/100 000 inhabitants [2], using the American-European Consensus Criteria [3]. The disease can also have extra-glandular features, with patients experiencing symptoms of pain, fatigue, neurological symptoms, sleep disturbance, autonomic dysfunction, low mood and an increased risk of developing lymphoma [4–13]. Consequently, many

patients experience reduced quality of life and difficulty with carrying out a range of daily activities [14, 15]. Furthermore, the disease is associated with significant direct and indirect healthcare costs equating to ~£12–15 000 per patient, per year [16, 17]. Similar figures have been identified in the USA [18]. European studies have identified increased physician visits and higher work disability for patients with a diagnosis of pSS [11, 19].

Non-pharmacological interventions for pSS may vary according to the particular symptom that they are targeting. They may be complex, target several symptoms at once and be conducted by more than one member of a multidisciplinary team [20]. Such interventions may include fatigue and mood management [11], and patient education by healthcare professionals [21]. Other interventions may be conducted by a clinician with specialist skills (such as occupational therapy to establish a balance in daily activities and improve function [22]), insertion of lacrimal punctal plugs for dry eye symptoms [23] or the use of acupuncture for the symptomatic relief of dry mouth [24].

Treatments in clinics for people with pSS tend to focus on pharmacological interventions. However, a recent systematic review has shown that evidence to support the efficacy of pharmacological therapies in pSS is poor [25]. Given the range of bio-psychosocial symptoms that these patients experience, it is possible that there are effective non-pharmacological treatments that could improve symptoms. The reduced impact of symptoms consequently may lead to an improvement in quality of life, improved work capacity and a reduction in economic costs to society. The objective of this study was to assess the effects of non-pharmacological interventions for pSS in adults.

Methods

All randomized controlled trials (RCTs) were included in this review. We included adult participants (over the age of 18 years) with a diagnosis of pSS. All non-pharmacological interventions that aimed to improve a symptom or symptoms of pSS were considered for inclusion. Pharmacological interventions are classified as medicinal products in accordance with EU Directive 2001/83/EEC (EU 2001), and these were excluded from the review. Homeopathic remedies, herbal medicines and trials of vitamins were regarded as pharmacological interventions for the purpose of this review and excluded, as the claimed mechanism of action is a chemistry change within the body. Comparison may be a placebo, alternative intervention that could be pharmacological or non-pharmacological or usual care. Outcomes considered within this review fell within the main domains addressed by the World Health Organization International Classification of Functioning Disability and Health [26].

Primary outcomes

Primary outcomes included assessments of activities of daily living, for example, the short-form (SF)-36 physical functioning scale and the improved HAQ; and participation

outcomes pertaining to work, return to work and social engagement, measured by, for example, The Work and Social Adjustment Scale.

Secondary outcomes

Impairment of body functions and structures included outcomes of mood, dryness, disease activity, daytime sleepiness, fatigue and cognitive function. Environmental factors included outcomes of costs, carer strain and willingness of employer to adapt work environment. Personal factors included self-efficacy level of education, adverse events and quality of life.

Search methods for identification of studies

There are a large number of possible non-pharmacological interventions, and each may have many synonyms. Initially, therefore, we performed a search for any RCT or controlled clinical trial for pSS. We combined the Medical Subject Headings (MESH) terms and keywords for SS with the Cochrane Highly Sensitive Search Strategy for identifying RCTs [27] (see supplementary data, search term section, available at *Rheumatology* Online).

The following electronic databases were searched from inception to September 2014: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Medline via OVID; EMBASE via OVID; PsycINFO via OVID; CINAHL via EBSCO; Current Controlled Trials Register (USA); World Health Organization International Clinical Trials Registry Platform; The National Research Register Archive (UK); and The UKCRN Portfolio Database (UK). In addition to the electronic databases, the references of included studies were also searched.

Two review authors (K.H. and V.S.) independently examined the title and abstract of all records identified, and full papers were retrieved for all papers that seemed to meet the inclusion criteria. All full-text articles were screened by two review authors independently (K.H. and K.D.).

Assessment of risk of bias

Two authors (K.H., K.D.) independently reviewed the studies for methodological quality, using the Cochrane Risk of Bias Tool [28]. Any discrepancies were easily resolved through discussion. Six items were used to assess risk of bias using only published material. Authors were contacted to seek clarification, but no replies were received, so a number of items remained unclear.

Results

The 14 publications that were subsequently excluded did not meet the review inclusion criteria: 8 were not RCTs, 5 did not report the pSS data separately for pSS participants and 1 study was an abstract only, with no reported outcomes (supplementary Table S1, available at *Rheumatology* Online). Twelve registered relevant clinical trials are either in process or have not yet published their findings (supplementary Table S2, available at

Rheumatology Online). The final selection, based on consensus, resulted in five trials being included in the review [29–33] (Table 1). See Fig. 1 for the flow diagram of included studies.

Risk of bias in included studies

See Fig. 2 for Risk of Bias Table. Sequence generation was judged to be at low risk of bias for two studies [32, 33] that used computer-generated randomization schemes. The method of sequence generation was not discussed in the remaining three included studies [29–31]. Concealment of allocation was judged to be at low risk in one study only [33]. Random allocations were placed in sealed opaque envelopes marked with study identification numbers by the same clinical staff. The remaining four studies did not include a discussion of allocation concealment.

Blinding was a limitation for all of the studies. In none of them were the participants masked as to the arm of the study they were in, and the masking was judged to be high risk. However blinding the participants to the interventions would have been difficult with the included non-pharmacological interventions. Detection bias was deemed to be low in one study [33], in which the staff performing the assessments and analyses were blinded to the treatment allocation. Two studies were judged to be at high risk of detection bias, as the outcome assessors were not blinded [29, 32]. The remaining two studies did not mention whether outcome assessors were blinded to treatment allocation.

Four out of the five included studies were at high risk of bias from incomplete outcome data. Follow-up measurements were not taken for all of the participants who took part in one study, and their baseline data were not presented in the analysis [29]. In a study on punctum plugs, six participants had spontaneous plug loss and a further participant had a reaction to the plug; thus, the data from these seven participants were excluded from the analysis [32]. Two participants were lost to follow-up in two separate studies, and their data were excluded from the analyses [30, 33]. In the remaining study [31], the data presentation was unclear, and it was not possible to determine whether the analysis was intention to treat.

We did not have access to the study protocols and were unable to assess this risk; thus, we have reported the parameter as unclear in four of the studies [30–33]. One study was judged to be at high risk of selective reporting [29], as an alexithymia measurement was taken only after treatment in the experimental group and was compared with baseline measurements from the control group in the analysis.

Participants

Overall, 130 participants with pSS were included in the studies. The number of participants with pSS in the studies ranged from $n = 42$ [33] to $n = 18$ [29]. All studies recruited both males and females, but the numbers of males recruited to each study were low and ranged from $n = 1$

Table 1 Summary of included studies

Study	Country	Description of intervention	Comparator	Participants	Quality	Results
Frost, 2006 [31]	UK	Intra-oral lubricating device	Treatment as usual	$n = 29$ Female = 27 Average age = 62 years	High risk of bias	Whole saliva and PUTTICA speech test improved. No difference in dryness outcome
List, 1998 [30]	Sweden	Acupuncture to increase salivary flow	Treatment as usual (waiting list)	$n = 21$ Female = 20 Average age = 65 years	Moderate risk of bias	Saliva production not stated. Mouth and eye burning not stated. No difference between groups
Mansour, 2007 [32]	Netherlands	Punctum plugs for dry eyes	Treatment as usual	$n = 20$ Female = 17 Average age = 55 years	High risk of bias	No data extractable. Unknown.
Poulsen, 1991 [29]	Denmark	Psychodynamic group therapy	Treatment as usual (waiting list)	$n = 18$ Female = 16 Average age = 54 years	High risk of bias	No difference between groups
Qiu, 2013 [33]	China	Punctum plugs for dry eyes	Eye drops	$n = 42$ Female = 36 Average age = 35 years	Low risk of bias	No difference between groups. Each group improved

Fig. 1 Flow diagram of study selection

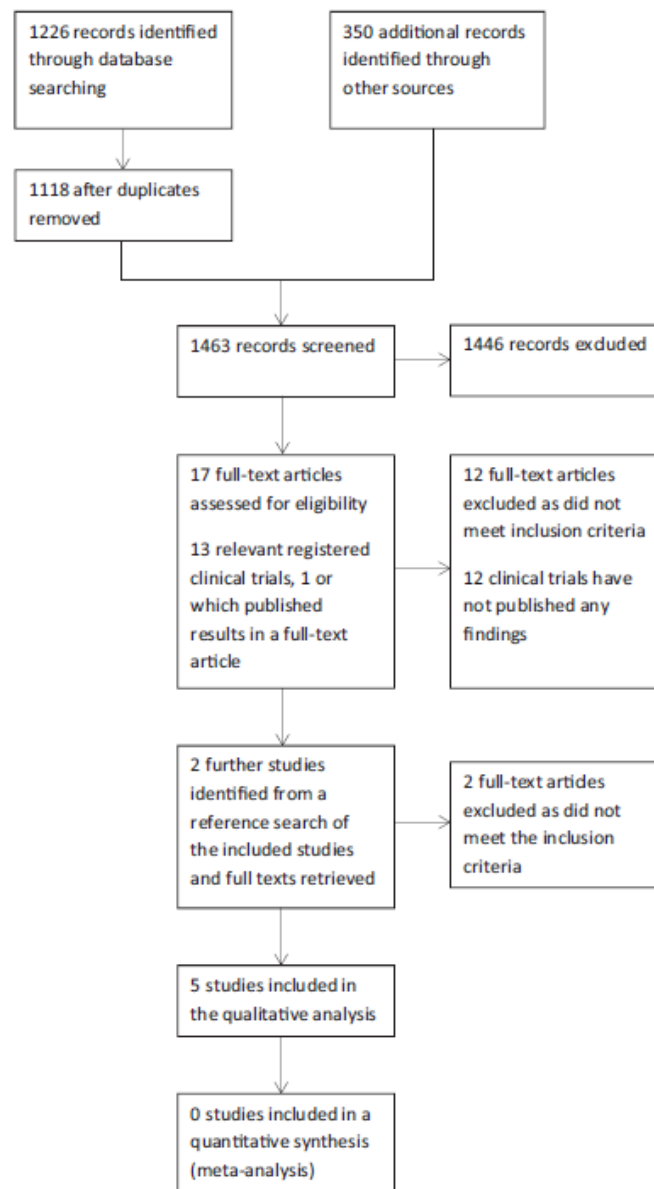
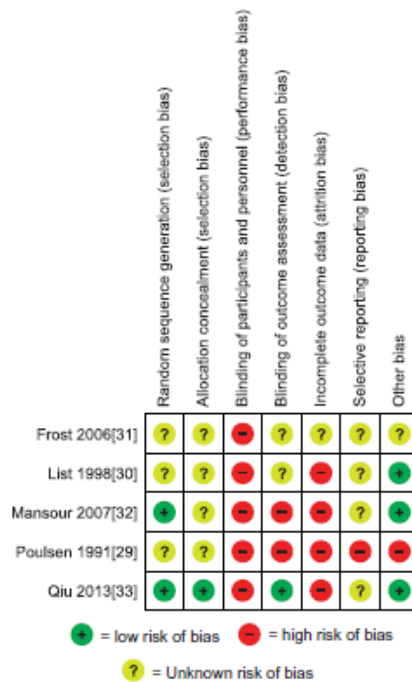


Fig. 2 Risk of bias summary: review of authors' judgements about each risk of bias item for each included study



[30] to $n=4$ [33], which is representative of the pSS population.

One study [30] included participants diagnosed with pSS according to the Copenhagen [34] and San Diego Criteria [35] and the proposed European Community Study Group Criteria [36]. The Qiu *et al.* [33] study reported that participants were diagnosed according to the American-European Consensus Criteria [3]. Mansour *et al.* [32] recruited participants diagnosed according to the European Criteria [36]. The remaining studies [29, 31] did not specify how the participants were diagnosed, although Frost *et al.* [31] did specify that they recruited their participants from a SS clinic (see supplementary Table S3, available at *Rheumatology* Online, for a summary of the main findings of these five selected studies).

Two of the five studies investigated punctum plugs for dry eyes [32, 33]. One study investigated an intraoral lubricating device for dry mouth [31], another investigated acupuncture for dry mouth [30] and the final study investigated psychodynamic group therapy [29].

A wide range of outcomes was assessed, and this is reflected in the outcome measures used. Four studies measured a range of outcomes relating to dryness

[30–33]. These included the following clinician-reported outcomes of unstimulated salivary flow over 10 min [30–33] and over 15 min [30] and paraffin-stimulated salivary flow over 5 min [30]. Further clinician-reported assessments of ocular dryness included tear gland function tests, including Schirmer's test [32, 33], the Rose Bengal test, mucus debris in the cul-de-sac [32], tear break-up time [33], ocular contrast sensitivity, glare disability and corneal fluorescein staining [33]. Further physician-reported oral dryness measures included the use of a 1–13 clinical dryness scale [31], an oral bacteriological sample and periodontal measurements (pocket depth, plaque and bleeding) [31]. Participant-reported outcome measures for dryness included discomfort from mouth dryness, eye dryness, tongue and mouth burning [10-point visual analogue scale (VAS)] [30] and subjective ocular discomfort [32].

Functional outcomes included a participant-reported questionnaire regarding the ability to speak, chew and swallow [31]; a 10-point VAS on both perceived global reduction in activities of daily living and the ability to chew and swallow [30]. One study used a speech test where the phoneme sequence PUTTICA was repeated as many times as possible over a 2-min period [31].

No serious adverse events were reported. One of the studies on punctum plugs reported spontaneous plug extrusion in 28% of the participants [32].

Effects of interventions

Primary outcomes

Qiu *et al.* [33] examined glare disability and visual acuity (ability to discriminate between two objects). Both the artificial tears and punctal plug groups demonstrated improvement for these two outcomes, but there was no significant difference between the two groups.

Frost *et al.* [31] examined speech function, but did not present baseline data; therefore, it is impossible to ascertain whether the difference observed between the two groups was due to the intervention, as there may have been a difference at baseline.

Poulsen [29] used the AIMS before and after psychodynamic group therapy. The AIMS is a self-reported questionnaire on physical functioning. However, the author did not report the actual results, and we are unable to comment on the reliability of this finding.

List *et al.* [30] asked patients to report the degree of reduction on their speech and chewing on a VAS at baseline and after a 10-week course of acupuncture. There was no significant difference between the control group and the intervention group at 10 weeks. In addition, participants in the same study were asked to report a global estimate of the reduction in daily activities on a scale of 0 to 10, with 0 meaning not at all and 10 meaning extreme. However, again there were no significant differences between the intervention group and control groups after 10 weeks.

The study by Poulsen [29] was the only one that measured participation as an outcome, and that study found no improvement in participation.

Secondary outcomes

Mansour *et al.* [32] asked participants to score eye discomfort on a 1–10 scale for both eyes. These measurements were taken at baseline and at follow-up, ~6 weeks after a silicone punctum plug was inserted into one of the eyes. However, the scale used was not validated, it was unclear how the scoring was conducted, and the sample size was very small ($n=13$). The authors did not report the differences between the control eyes and the plugged eyes. Despite the small sample size, we have reanalysed their reported data with a two-tailed unpaired *t*-test in order to determine differences between the groups at follow-up. There were no significant differences between the control and intervention groups at follow-up ($P=0.2416$).

Qiu *et al.* [33] conducted Schirmer's test to determine dryness of the eyes before and after treatment, and both groups improved; although the authors claim the plug group improved significantly more than the artificial tear group, they did not present the analysis that supported this claim. We have reanalysed their data and can confirm that it was significant ($P<0.001$).

Frost *et al.* [31] presented no baseline data; therefore, their results on the use of oral lubrication devices were not interpretable.

Poulsen [29] reported improvements in alexithymia (difficulty in identifying and describing emotions) scores 9 months after taking part in psychodynamic group therapy, despite not measuring the scores at baseline for the intervention group.

List *et al.* [30] asked participants to evaluate mouth dryness, eye dryness and burning sensation in the mouth on a VAS at baseline and after a 10-week course of acupuncture, but there were no significant differences between the intervention and control groups. None of the studies measured quality of life, self-efficacy or environmental factors such as carer strain and costs.

Discussion

Overall, the quality of the included studies was poor. There was high risk of bias in most, and none had conducted power calculations. Furthermore, the sample sizes used were small, meaning the studies were likely to be underpowered for detecting an effect size that was predicted to be modest.

The quality of reporting was also poor; in particular data presentation, which made data interpretation difficult. For example, no baseline data were reported in two of the studies [29, 31], and one of these reported improvements in an outcome but presented no supporting data [29]. None of the included studies conducted the appropriate analysis of change in scores, or the analysis of difference between the two groups. Instead, baseline to study end-point scores were reported.

Overall, our findings were inconclusive. These studies suggest that punctal plugs are effective for outcomes of body function and some activity outcomes. This is in line with a Cochrane review of punctal plugs in dry eyes [37], which was not pSS specific. The oral lubrication devices,

psychodynamic therapy and acupuncture did not provide evidence of significant benefit. However, given the poor quality of the data presented and the small sample size, we cannot be certain that these interventions provide no benefit either.

The studies included some measures of glandular function, including damage to the eyes and some measures of activities. Of the activity measures, not all related to everyday life. An example is the PUTTICA speech test [31], which is a surrogate outcome with an unclear relationship to intelligibility or ease of speech. Only one study looked at any aspects of participation [29], and there appears to be a lack of appropriate outcome measures that are relevant to patients in terms of activity and participation. Studies investigating body function and structure outcomes need to determine the relevance of these outcomes to patients and to investigate the impact of such symptoms on participation, the ability to perform daily activities and quality of life.

We discovered no published reports of RCTs of studies looking at exercise or cognitive behavioural therapy, which have been examined in chronic fatigue syndrome studies [38]. A small study investigating a group aerobic exercise intervention (Nordic walking) [39] was not eligible for inclusion, as participants were not randomized and it is difficult to determine evidence of efficacy in non-randomized trials [40].

Through a search of clinical trials databases, we were able to determine that there were 13 relevant clinical trials; however, only one of these had published results [32]. A RCT has been registered in the Netherlands, investigating cognitive behavioural therapy and exercise training to treat fatigue in SS and non-SS sicca syndrome [41], but no results have yet been published. Further research is recommended into clinically relevant non-pharmacological interventions for which there is evidence of efficacy in other conditions with similar symptoms; such as cognitive behavioural therapy and graded exercise therapy for fatigue management in patients with chronic fatigue syndrome.

A Cochrane systematic review of punctal plugs for dry eyes concluded that they provided some symptomatic relief in severe dry eyes, and it is likely that they would be of benefit in pSS as well as in other dry patient groups. Further investigation into any differences between pSS dry eye treatment and standard dry eye treatment is warranted.

Conclusion

Overall, we identified no current evidence to support any non-pharmacological interventions to improve the quality of life for people with pSS. The area needs good quality, appropriately powered RCTs that are reported according to Consolidated Standards of Reporting Trials guidelines. Outcomes should be sensitive to changes that are important and relevant to patients.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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Open Access

Protocol

BMJ Open Developing a service user informed intervention to improve participation and ability to perform daily activities in primary Sjögren's syndrome: a mixed-methods study protocol

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ABSTRACT

Introduction: A significant proportion of patients with primary Sjögren's syndrome (PSS) is functionally impaired and experience difficulties participating in various aspects of everyday life. There is currently no evidence of efficacy for non-pharmacological interventions aimed specifically at supporting the patients with PSS to improve their participation and ability to perform daily activities. This paper describes a research protocol for a mixed-methods study to develop an intervention to improve these outcomes. The protocol follows the Medical Research Council framework for complex interventions.

Methods and analysis: We will use group concept mapping with the patients, adults who live with them and healthcare professionals to identify factors which prevent people with PSS from participating in daily life and performing daily activities. The factors will be prioritised by participants for importance and feasibility and will inform an intervention to be delivered within a National Health Service (NHS) setting. Evidence-based intervention techniques will be identified for the prioritised factors and combined into a deliverable intervention package. Key stakeholders will comment on the intervention content and mode of delivery through focus groups, and the data will be used to refine the intervention. The acceptability and feasibility of the refined intervention will be evaluated in a future study.

Ethics and dissemination: The study has been approved by an NHS Research Ethics Committee, REC Reference: 13/NI/0190. The findings of this study will be disseminated in peer-reviewed journals and through presentation at national and international conferences.

Trial registration number: UKCRN Study ID: 15939.

BACKGROUND

Primary Sjögren's syndrome (PSS) is an autoimmune rheumatic condition which a recent meta-analysis has identified as having a

Strengths and limitations of this study

- This study will allow people with primary Sjögren's syndrome, their families and healthcare professionals to identify and prioritise key factors or barriers to participation and daily activities.
- This information will allow us to develop an evidence-based intervention to improve participation and the ability to perform daily activities for people with primary Sjögren's syndrome.
- This study will result in an intervention package and a feasibility study protocol in readiness for testing the intervention for acceptability and feasibility within a National Health Service setting.

prevalence rate of 74/100 000 inhabitants¹ using the American European Consensus Criteria (AECC).² In addition to the classic symptoms of oral and ocular dryness, arthralgia and myalgia,³ the patients with PSS experience significant fatigue,⁴ sleep disturbance,⁵ autonomic dysfunction⁶ and a markedly reduced quality of life (QOL).⁷ Furthermore, PSS is associated with significant direct and indirect healthcare costs equating to around £12–£15 000 per patient per year.^{8,9}

We recently conducted a literature review on the impact of PSS on participation and the ability to perform daily activities and concluded that many patients with PSS are restricted in their ability to participate in various aspects of everyday life and are functionally limited, which is affecting their ability to carry out daily activities.¹⁰ Consistently, using the Improved HAQ, a validated instrument for assessing ability to perform daily activities, we demonstrated that people with PSS have significant

impairment that is comparable with those with chronic fatigue syndrome.¹¹

We also conducted a systematic review of non-pharmacological interventions for PSS which identified very few studies in the literature and concluded that there was no current evidence for the effectiveness of non-pharmacological interventions for PSS.¹² Current medical care for the patients with PSS has mainly focused on pharmacological interventions for their classic symptoms, which at best are only partially effective.¹³ Currently there is no evidence of efficacy for non-pharmacological interventions aimed at improving participation and the ability to perform daily activities for the patients with PSS. This is in contrast to patients with other long-term conditions such as cancer, chronic fatigue syndrome and chronic pain who have access to psychosocial therapies which have been shown to improve symptoms and functional ability.^{14–17} Therefore, there is a need to develop effective interventions to improve function and participation in everyday activities for people with PSS.

In order to develop an effective intervention that is deliverable in the UK's National Health Service (UK NHS), it is important to understand what the key issues are for service users, their families, healthcare professionals and those who commission and manage NHS services for the patients with PSS. This will maximise the likelihood that the intervention addresses important issues and is feasible and acceptable. The Medical Research Council (MRC) framework for complex interventions¹⁸ advises an iterative stepped, structured and mixed-methods approach. At the early stages, when little is known regarding the determinants of illness and illness-associated impairments, a combination of qualitative techniques to explore patient experience and a review of the existing evidence is recommended. Such findings will then form the theoretical and empirical basis for developing an intervention specific for PSS. The key tasks are to identify intervention targets, the mechanisms whereby the proposed intervention will lead to change in participation and the ability to perform daily activities. Furthermore, recommendations will be made for specific measures to be used.

While the MRC guidance provides a useful framework for intervention development, it is less clear on the exact methods to achieve this. A variety of methods from economic modelling to computer simulation have been suggested, many of which may not be applicable to complex psychosocial interventions. In this regard, group concept mapping (GCM) methodology has been used to good effect for strategic complex planning in other diseases including dementia¹⁹ in addition to intervention planning and treatment decisions in cancer.^{20, 21}

GCM, developed by Trochim,²² is a mixed-methods participatory approach that uses a combination of group processes (brainstorming, sorting, rating and group interpretation) and a sequence of multivariate statistical analysis (multidimensional scaling and hierarchical cluster analysis) that result in visual representations of all stakeholders opinions in the form of concept maps.

Priority values are added by participants to qualitative statements gathered during the brainstorming phase and these can be interpreted in pattern matches and value plots and used in planning or evaluation studies.²³ An advantage of GCM over some other methods is that it is an equitable process, giving an equal voice to all stakeholder groups and does not direct the participants to form a consensus. In the rheumatology field GCM has been used to design interventions to prevent work disability in patients with rheumatoid arthritis²⁴ and to understand their work requirements.²⁵

In this study, we will identify priorities and intervention strategies that could improve participation and the ability to perform daily activities for people with PSS. The findings of the GCM exercise will be used to identify priority factors or targets, which are perceived to prevent the patients with PSS from participating in daily activities. Furthermore, the chosen factors will be measurable and tools selected to measure change for each. Existing evidence for each identified factor will be identified from the literature as the basis for the development of an intervention package aimed at improving daily function for people with PSS. The results of the concept maps and the planned development package will be discussed in focus groups of the patients with PSS, their family members or supporters and generic occupational therapists working in the UK NHS. The planned intervention will be further refined, drawing on feedback from those who will be at both the receiving and delivery ends of the proposed intervention.

At the conclusion of this study a detailed feasibility protocol will be drawn up following the proposed CONSORT reporting guidelines for feasibility and pilot studies²⁶ and ethical approvals will be sought. The intervention will subsequently be tested for feasibility on a small number of the patients with PSS in an NHS setting in a future study.

Although the project is primarily aimed to develop an intervention for use in UK NHS settings, its findings may be useful for other publicly funded health services or private healthcare providers.

AIMS AND OBJECTIVES

Aim

To build a model for intervention in PSS.

Objectives

1. To collect data from different stakeholder groups for priority intervention target areas in PSS.
2. To use existing clinical evidence to establish the optimum intervention and mechanism of effect of intervention for selected intervention targets.
3. To use existing clinical evidence to identify outcome measures best suited to capturing intervention effect.
4. To establish which of these priority areas could be realistically delivered within a UK NHS setting.
5. To design protocol for a future feasibility study of the refined intervention.

METHODS AND ANALYSIS

We will use GCM to explore the perspectives of three stakeholder groups on what will improve functional capacity of the patients with PSS. The stakeholder groups will be patients with PSS, adult household members (here onwards referred to as 'family') who live with someone who has PSS and healthcare professionals, managers and commissioners (here onwards referred to as 'providers') involved in the care delivery or service provision for patients with PSS.

Sample size

The recommended minimum number of participants for a GCM exercise is $n=40$.²⁷ We will seek to recruit approximately $n=280$ participants in order to enable subgroup analyses and to allow for modest attrition rates at each step of the GCM exercise (see figure 1). We aim to recruit 50 providers, 50 family members and 180 patients with PSS. This will allow us to detect a difference of the same order of magnitude as the background variability with 80% power. Subgroups within the patient group will allow us to compare opinions of the patients with PSS with varying levels of fatigue, QOL, perceived dryness, pain, cognitive symptoms and mood disturbances.

Recruitment

Patients who are participants in the UK Primary Sjögren's Syndrome Registry (UKPSSR)²⁸ and have consented to be approached about further studies will be invited to take part in this study via a postal invitation.

Up to 12 patient identification sites across England will be used to identify potential participants. Family members will be invited to participate in an invitation addressed to an adult household member in the patient invitation pack. Providers will be invited to participate at professional meetings and through email invitation via email distribution lists.

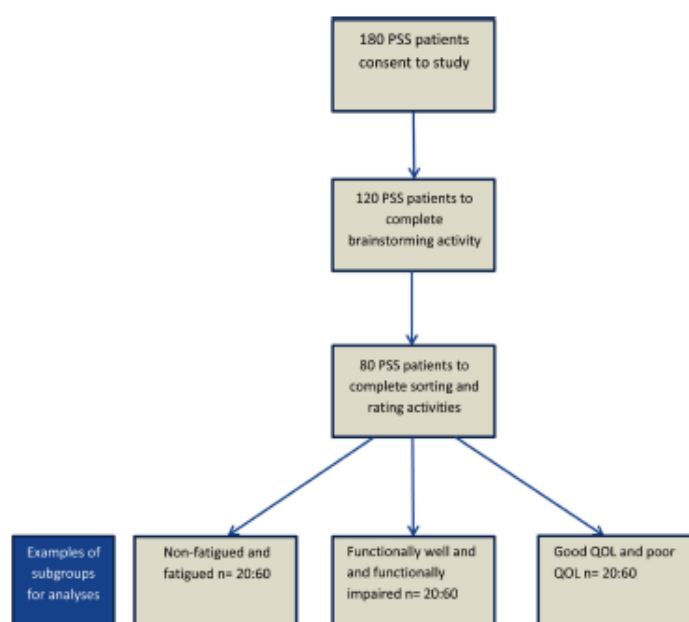
Consent

The participants will be sent an invitation pack in the post. Within the pack will be a participant information sheet, a consent form and a reply form. They will be asked to reply to the invitation, indicating on the reply form whether they would like to participate. They will be provided with a telephone number and an email address to contact the research team if they have any questions. Once any queries have been satisfied they will be asked to sign, complete and return the consent and reply forms.

Data collection

Baseline demographics will be collected from all the participants (see figure 2). The PSS group will be asked to complete self-assessment on mood, QOL, function, fatigue, cognitive symptoms, dryness, discomfort and pain using validated instruments (see figure 3). This will allow us to perform subgroup analyses and compare whether opinions differ or not within the patient group. For example comparisons of the patients who are functionally impaired with those who are not; or those who are fatigued and those who are not. Family members will be asked to complete short validated questionnaires to

Figure 1 Flow chart of the participants to be recruited to the PSS participant group (PSS, primary Sjögren's syndrome; QOL, quality of life).



measure the impact of their spouse/relative's disease on them as well as their own QOL, as this may influence their opinion in the concept mapping exercise, regarding what they feel as priority areas for a healthcare intervention. Health care professionals (HCPs) will be asked to indicate which professional group they belong to. These data will allow us to perform additional subgroup analyses within the family and provider groups.

BUILDING A MODEL FOR INTERVENTION IN PSS

GCM phase

Identifying factors: idea generation/brainstorming

We will seek open contribution of ideas from each stakeholder group in response to a focus prompt. A focus prompt is an incomplete sentence designed to elicit ideas from the participants during the brainstorming

phase of a GCM exercise. To generate a range of factors, the participants will be asked to complete the following focus prompt:

People with primary Sjögren's syndrome would be able to do more of the things they want to do and the things they have to do if...

The participants will be asked to think and record as many responses as they can during this process.

Ideas analysis

All statements will be analysed and synchronised by a study advisory group consisting of representatives of all stakeholder groups and the research team. We will use a structured process recommended by Kane and Trochim²³ to remove duplicate statements and ensure

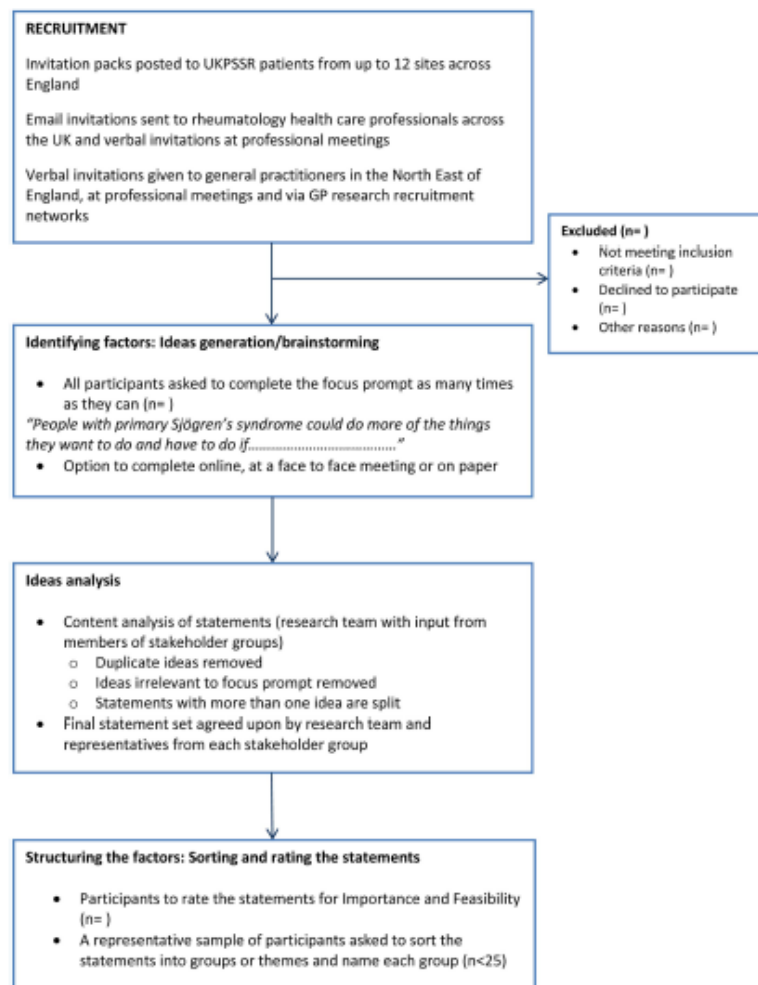


Figure 2 Flow chart of concept mapping study (GP, general practitioner; UKPSSR, UK Primary Sjögren's Syndrome Registry).

Questionnaires

- Patients with PSS (n=)
 - Demographic questions*
 - Pain (Comprehensive pain evaluation questionnaire (CPEQ), visual analogue scale (VAS))
 - Fatigue (Profad-F, VAS and adapted CPEQ**)
 - Mental fatigue (VAS and adapted CPEQ**)
 - Functional disability (Improved Health Assessment Questionnaire)
 - Dryness (VAS and adapted CPEQ**)
 - Mood (HADS, VAS and adapted CPEQ**)
 - Cognitive impairment (Cogfall)
 - Quality of Life (SF-36)
- Adult Household Members (n=)
 - Demographic questions*
 - Quality of Life (SF-36)
 - Carer strain (Carer Strain Index)
- Health Care Professionals (n=)
 - Demographic question (job role)

* Demographic questions for AHM group

- Age, gender, years since PSS diagnosis, education level, employment status

* Demographic questions for PSS group

- All the above plus education level, household income, and receipt of benefits

** The activity interference grid from the CPEQ has had the word "pain" replaced the words "fatigue", "mood" (anxiety or depression), "dryness" and "brain fog or mental fatigue" to determine how these factors impact on daily activities

Figure 3 Measures to be used during the concept mapping phase (AHM, adult household member; HADS, Hospital Anxiety and Depression Scale; PSS, primary Sjögren's syndrome). **The activity interference grid from the CPEQ.

wording is clear. This will condense the statement set to one which is of manageable size (≤ 96 statements)²⁷ for the subsequent sorting and rating exercise but large enough to ensure saturation of the topic.^{22 27}

Structuring the factors: sorting and rating the statements

The participants who previously took part in the brainstorming exercise will be invited to take part in the sorting and rating phase. Some participants may be recruited solely to the sorting and rating phase if saturation of the brainstorming topic is achieved prior to recruiting the planned number of participants, or if there is significant participant attrition between the two phases of the study. The participants will be asked to rate each statement in the distilled set on a five-point rating scale for importance and feasibility. When asked about feasibility they will be asked to consider how

realistic it is to address the particular issue presented by the statement in an NHS setting. Next they will be asked to sort the statements into themes or groups of similar statements or ideas.

Procedures for the concept mapping phase

The patients with PSS and AHMs will be given the option of participating in the concept mapping exercises via one of the following means: (1) face-to-face focus groups of 5–10 people (if they live within 10 miles of the research centre), (2) a web-based interface or (3) paper-based questionnaire. HCPs will participate via the online web-based interface or on paper-based questionnaires. The participants completing the web-based concept mapping exercise will be given a unique username (not their name) and password.

In the group brainstorming session, a trained facilitator may use neutral prompts if ideas start to dry up. The participants also have the option of completing their responses on a piece of paper and handing it to a facilitator if they do not feel comfortable verbalising their responses. In the online format, the participants will be able to see the anonymous responses of the participants who have already completed the brainstorming process, which may help to prompt their own ideas. The participants choosing to complete the exercises on paper via the post will have a blank piece of paper to record their ideas on and will not have the benefit of seeing other peoples' responses.

When conducting the sorting and rating exercises, the participants may choose a different method to their chosen one for brainstorming if they wish. For example, they may complete the sorting and rating exercise online if they attended a face-to-face meeting for brainstorming. Furthermore, the participants may take part in sorting or rating even if they did not originally undertake the brainstorming exercise.

Concept mapping analysis and interpretation

The data generated from the above exercises will be analysed and represented in objective form as visual maps using the Concept Systems Global software package.

The maps will highlight the priority areas for each stakeholder group in improving function of the patients with PSS. Similarities and disparities between the stakeholder groups can be identified and if appropriate subgroup analyses will be carried out using the baseline demographic data collected at the start of the study and the self-assessment data. The "go zones" represent areas that are of most importance for more than one stakeholder group and so are of particular importance for planning interventions.

Intervention development phase

The key barriers or factors identified in the GCM exercises will be used as the basis for developing interventions and selecting appropriate measures which can be used later for a formal evaluation of effectiveness. We

will use an existing, reportable method described by Kolehmainen and Francis²⁹ to identify the techniques to be used in the intervention and will review existing literature to identify the measures. This involves three steps.

First, potential intervention techniques (active ingredients) will be identified from existing literature and relevant evidence-based theories. These will be identified in relation to the prioritised factors. Where the literature to indicate a technique for a factor is scarce, evidence-based theories from related fields, such as behaviour change will be used. Existing tools such as a matrix of behaviour change techniques³⁰ enable systematic identification of techniques from these fields. Second, the factor is specified as an observable and measurable 'construct' and a measure for identifying change in it will be selected. Third, each technique and factor pair is presented as a testable hypothesis in relation to the primary outcome.

An illustrative example of the application of this three-step method is shown below.

Illustrative example: potential factor—chronic fatigue

Evidence-based intervention techniques to target chronic fatigue include, grading physical activity/exercise¹⁵ and goal setting, biofeedback and body changes.³⁰ Chronic fatigue is commonly measured as the self-reported mental and physical tiredness, by using tools such as the Chalder Fatigue Scale³¹ or the Profile of Fatigue.³² The testable hypothesis may be articulated as "grading, goal setting, biofeedback and body changes can be used to reduce chronic fatigue in order to increase participation in meaningful occupations."

The intervention will be reported using the Template for Intervention Description and Replication (TIDieR).³³

Intervention refinement phase: focus groups

Once the potential intervention techniques have been identified from the literature, these will be presented to people with PSS, their families and occupational therapists in focus groups. The focus groups will provide opportunities to gather feedback regarding the specific intervention techniques, how the techniques will be best delivered and measures of effectiveness. The participants will be asked to generate ideas regarding how to deliver the techniques in an effective and acceptable way. Patient and carer participants will be identified from a regional specialist medical service for PSS and will be those who have previously indicated an interest at being involved with further research. Potential therapist participants will be recruited from local hospitals and community-based occupational therapists.

In addition the focus group participants will be invited to comment on the proposed outcome measures, including the choice of instrument(s) and the processes of administering and completing these instrument(s). The results will be used to refine the intervention package.

Designing a feasibility study

Once the intervention has been designed and the measurement tools identified, a detailed protocol following CONSORT guidance³⁵ will be drawn up and ethical approvals sought. This will form the next stage of the intervention development process.

ETHICS AND DISSEMINATION PLAN

This study has received approvals from the Office for Research Ethics Committees Northern Ireland (Ref: 13/NI/0190) and has been adopted onto the UK Clinical Research Network Study Portfolio (UKCRN Study ID: 15939). The results from both the concept mapping phase and an outline of the refined intervention will be disseminated nationally and internationally and submitted to scientific journals for publication.

SUMMARY

This study seeks to identify important factors from the patients with PSS, their families and providers regarding what could improve participation and the ability to perform daily activities for people with PSS. The identified factors will be targets for specific evidence-based intervention techniques and appropriate measures will be identified for each. This will result in an intervention package which will be refined in focus group discussions with key stakeholders. The next stage of the intervention development process will be a feasibility study of the refined intervention and this will be the subject of a future protocol.

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Hackett, K., Newton, J., Rapley, T., Deane, K., Deary, V. and Ng, W.F. (2014)
'Systematic reviews of occupational therapy interventions: summarizing
research evidence and highlighting the gaps', ***British Journal of Occupational
Therapy***, 77(9), pp. 479-482.

Systematic reviews of occupational therapy interventions: summarizing research evidence and highlighting the gaps

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Key words:

Review literature as topic, evidence-based practice, review, systematic.

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As services are commissioned based on effectiveness, occupational therapists are under pressure to demonstrate the efficacy of their interventions. Occupational therapists also need to know that the interventions they are providing are effective. Robertson et al (2013) demonstrated that the occupational therapy literature is important for clinicians and is an essential part of their practice. However, as more research is published, it can be increasingly time-consuming and confusing for clinicians to keep abreast of the current literature. Occupational therapy-related research may be published in different forms, in a range of locations, and be of varying methodological quality. Furthermore, readily available published studies that investigate occupational therapy efficacy may not be sufficiently powered, or may lack external validity, when applied to different clinical settings. When well conducted, systematic reviews provide a useful way of synthesizing and evaluating the evidence on a particular topic and, to some extent, provide a solution to this problem. This paper focuses upon reviews of randomized controlled trials, as these provide the highest quality of evidence on the question of a particular intervention's effectiveness. The merits of reviews of qualitative studies are also considered, together with the possibility of combining more than one type of review.

Background

The Cochrane Library holds the open access peer-reviewed *Database of systematic reviews* (The Cochrane Collaboration 2013a) and currently includes several completed reviews of occupational therapy. In addition, systematic reviews of occupational therapy, or interventions relevant to the field of occupational therapy, are published in a range of peer-reviewed journals (Bennett et al 2013), including occupational therapy, social science, psychology, medical, and rehabilitation publications. In August 2013, the OTseeker database (Bennett et al 2007) listed 1,285 systematic reviews, collated from a wide range of journal types, relevant to the field of occupational therapy. Over the last decade, there has been a sharp increase of published systematic reviews, and prospective registration is advised to ensure transparency in review process and outcomes (Booth et al 2011). Clear guidance is available for conducting a systematic review of interventions (Higgins and Green 2008), and the PRISMA statement provides guidelines on how to report them (Moher et al 2009). Robust reviews, conducted and reported in such a way, can provide a summary of the available evidence on a topic, according to specific inclusion and exclusion criteria; they can, in turn, inform clinicians and policy makers, leading to the development of local and national guidelines. The College of Occupational Therapists' [COT] *Practice guidelines development manual* (COT 2011), accredited by the National Institute of Clinical Excellence (NICE), recommends a systematic approach to reviewing the literature when developing occupational therapy guidelines.

A potential criticism of performing systematic reviews of occupational therapy interventions is an absence of good-quality randomized controlled

trials. Subsequently, it is possible that a systematic review may be 'empty', where either no studies are included, or in the absence of studies of sufficient quality, occupational therapy cannot be recommended (Deane 2006). However, one might also conclude that a gap in the literature, highlighted by a systematic review, provides a useful reference point for designing a study of effectiveness following CONSORT guidance (Schulz et al 2010). Furthermore, the results of a systematic review that demonstrates evidence gaps or the need for more research in a specific area can provide a valuable summary for submission of a grant application, and identify a need for further research. Where there are sufficient numbers of good-quality, homogeneous studies included within a review, the results of the studies can be combined in a meta-analysis, which is the statistical pooling of data from two or more studies.

Meta-analysis can demonstrate larger effect sizes where there are low participant numbers within each included study. However, as occupational therapy is a complex intervention (Creek et al 2005), it is likely that there will be sufficient heterogeneity amongst the included studies to make a meta-analysis at best meaningless, and at worst misleading. In many cases, a narrative synthesis will be more appropriate. A narrative synthesis of included studies tells a trustworthy story and is an approach to combining the findings of the included studies. Text and words are primarily used to describe and summarize the studies and their results (Popay et al 2005). Murphy et al (2009) have highlighted some specific considerations for systematic reviews of occupational therapy interventions. These include the inclusion of relevant papers and the evaluation of papers with an expanded hierarchy of evidence.

What is a systematic review?

A systematic review asks a 'clearly formulated research question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarize the results of included studies' (The Cochrane Collaboration 2013b). A systematic review, therefore, presents the available high-quality evidence on a particular subject in a concise and digestible form.

An overview of the review process

The Cochrane handbook for systematic reviews of interventions (Higgins and Green 2008) provides detailed instructions on each stage of a systematic review. The following is a brief overview of the stages involved.

Prior to starting a review, it is important that time and resources, including access to relevant databases, full-text access of papers, and library access for interlibrary loans, are available. A dedicated team of reviewers with defined roles is required, and team members need to have a range of experience and

expertise. The research question needs to be considered and structured around the population, intervention, comparator, and outcomes. During the preparation phase, the scope is finalized and the protocol developed and registered with the international prospective register, the PROSPERO (Centre for Reviews and Dissemination [CRD] 2013).

To minimize bias, each review stage should be conducted by at least two people. The search of each of the predetermined databases, using predefined search terms, will reveal the papers for consideration in the review. The titles and abstracts may be combined within a reference manager library for ease and any duplicates removed. A robust search strategy is essential to ensure no relevant studies are missed. References of all included studies should be checked for further potentially relevant studies, and authors of included studies contacted for further details. Finally, a search of grey or unpublished literature is recommended (Higgins and Green 2008). This may include theses, trials databases, and conference abstracts.

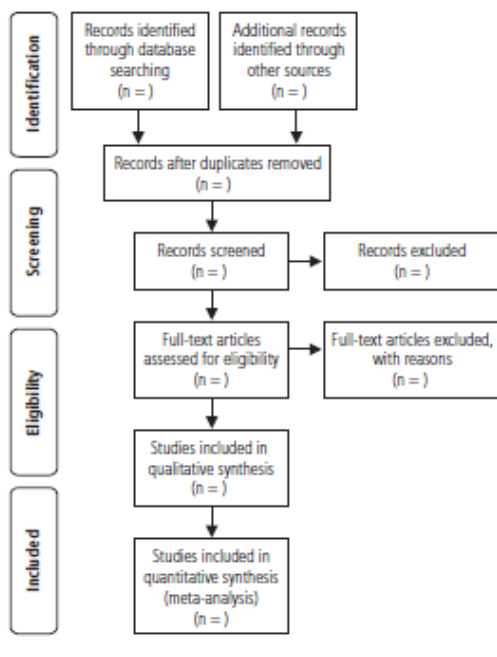
Studies are selected according to the inclusion and exclusion criteria in the protocol. Initially, the selection is made on the basis of study title and abstract. The full text of papers highlighted by this process are retrieved and read, whilst being considered for inclusion against the predetermined criteria. The quality of each included study must be assessed, according to the assessment tool highlighted in the protocol, which assists with maintaining objectivity in the review. The data from each study are then extracted into tables.

Combining the results of several studies creates larger samples and yields more robust results than would be possible from any single study. It increases the power and may also increase the external validity due to the variation in the studies. A meta-analysis may be performed if appropriate, ideally after a narrative analysis. Access to a statistician is advisable, particularly if a reviewer is unfamiliar with types of data and effect measures.

Disseminating the review

The PRISMA statement (Moher et al 2009) provides guidance for reporting a systematic review, and provides a checklist and flow diagram (see Fig. 1). To give a clear overview, in a standardized format, of all studies screened, assessed for eligibility, and included in the review. The reasons for excluding studies are reported, making it possible to see why a particular paper was not included. The PRISMA checklist for abstracts (Beller et al 2013) gives helpful guidance for the preparation of conference or journal abstracts. Additionally, a report should be submitted to the funder and perhaps to the organization in which it was carried out, such as the hospital trust. A systematic review may also form the whole or part of a thesis, and later be prepared in a suitable format for journal submission. Many journals, including the *British Journal of Occupational Therapy*, welcome the submission of high-quality systematic reviews relevant to the journal's subject area.

Fig. 1. PRISMA flowchart template for a systematic review (Moher et al 2009).



Further considerations

Systematic reviews of qualitative research can give readers access to topics such as patient/client and practitioner experiences of, or the barriers and facilitators to, implementing an occupational therapy intervention. They move beyond summarizing data, synthesizing individual qualitative research studies 'that relate to a specific topic or focus in order to arrive at new or enhanced understanding about the phenomenon under study' (Paterson 2012). However, synthesizing qualitative and quantitative evidence can be challenging, and a range of approaches are available (Dixon-Woods et al 2005). Tomlin and Borgetto (2011) presented an evidence-based practice model that outlines the synthesis of a range types of evidence, including syntheses of qualitative studies, meta-analyses of both experimental and outcome research, and systematic reviews of descriptive studies. They proposed that the highest level of evidence would be a 'mega-synthesis'. While this may seem challenging, their three-sided pyramid model of occupational therapy evidence can guide practitioners in reaching decisions about their services or interventions.

Often, the first time that a clinician may conduct a systematic review is during postgraduate research. However, as research is becoming more important within clinical roles, and as therapists may pursue a research career pathway, reviews may be conducted within clinical and academic settings in multi-disciplinary teams. An occupational therapist may be

invited to be part of a review team due to their clinical skills, despite having little previous practical experience of the review process.

Occupational therapy practitioners and academics should actively seek to form teams that address the areas of need highlighted by practitioners. For occupational therapists with little experience of the review process, it is important to become familiar with the steps identified above and to identify a mentor with experience of the review methodology. Accessing appropriate training in conducting systematic reviews and gaining critical appraisal skills would mean that a potential reviewer has the expertise required to undertake such research.

Conclusion

In recent years there has been an increase in the number of published systematic reviews applicable to occupational therapy (Bennett et al 2013). Rigorous systematic reviews are useful for clinicians, commissioners, and policy makers. When a review demonstrates gaps in the evidence, this may provide a case for further research and can be useful when submitting funding applications. Systematic reviews should be conducted in a transparent way, with the protocol published in an accessible database prior to the review process commencing. Whilst this opinion piece has primarily focused on quantitative reviews, other types of systematic reviews and syntheses can also inform occupational therapy practice. Occupational therapists may conduct systematic reviews as part of their role, and clinical and academic occupational therapists should consider forming review teams to combine their specialist knowledge. Training courses are helpful, following appropriate guidance is essential, and it may be useful to identify a mentor for guidance with the process.

Acknowledgements

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A.4.2 Other publications

A.4.2.1 Co-authored peer reviewed publications

Price, E., Rauz, S., Sutcliffe, N., Hackett, K.L., Barone, F., Granata, G., Ng, W-F., Fisher, B.A., Bowman, S., on behalf of the BSR and NHPR Standards, Guideline and Audit Working Group (2017) 'BSR and BHPR Guideline for the Management of Adults with Primary Sjögren's Syndrome' ***Rheumatology (Oxford)*** (*In press*).

Syla, D., Sweenie, A., Lendrem, D., Newton, J.L., Hackett, K.L. (2017) 'A scoping exercise to gauge the incidence of early post stroke fatigue for patients at Newcastle Community Stroke Services' (letter) ***International Journal of Therapy and Rehabilitation*** (*In press*).

Hart, R.I., Ng, W-F., Newton, J.L., Hackett, K.L., Lee, R.P., Thompson, B. (2016) 'What impact does written information about fatigue have on patients with auto-immune rheumatic diseases? Findings from a qualitative study' ***Musculoskeletal Care*** (*ahead of print*).

Howard-Tripp, N., Tarn, J., Natasari, A., Gillespie, C., Mitchell, S., Bowman, S., Price, E., Pease, C.T., Emery, P., Andrews, J., Lanyon, P., Hunter, J., Gupta, M., Bombardieri, M., Sutcliffe, N., Pitzalis, C., McLaren, J., Cooper, A., Regan, M., Giles, I., Isenberg, D., Saravanan, V., Coady, D., Dasgupta, B., McHugh, N., Young-Min, S., Moots, R., Gendi, N., Akil, M., Hackett, K.L., Griffiths, B., Lendrem, D. and Ng, W-F. on behalf of the UK primary Sjögren's Syndrome Registry. (2016) 'Fatigue in primary Sjögren's syndrome is associated with lower levels of pro-inflammatory cytokines' ***RMD Open***, DOI:10.1136/rmdopen-2016-000282

Lendrem, D., Mitchell, S., McMeekin, P., Gompels, L., Hackett, K., Bowman, S. et.al. (2015) Do the EULAR Sjögren's syndrome outcome measures correlate with health status in primary Sjögren's syndrome? ***Rheumatology (Oxford)***, 54(4):655-9.

A.4.2.2 Non-peer reviewed publications

Hackett K.L. (2016) 'Being part of a group to develop new national guidelines for the clinical management of primary Sjögren's syndrome: A reflective account' (2016) ***Journal of Rheumatology Occupational Therapy*** 30(1), pp. 22-23.

Bannigan, K., Birken, M., Hackett, K.L. (2016) 'Complex interventions; the latest thinking: Designing and evaluating complex interventions in health and social care: highlights from a recent conference' ***Occupational Therapy News***, February, pp. 22-23.

Lambson, R.L., Newton, J.L., Strassheim, V., Gotts, Z., Deary, V. and Hackett, K.L. (2015) 'The evolution of the Newcastle CRESTA Fatigue Clinic: a unique NHS multidisciplinary approach to fatigue', ***Journal of Rheumatology Occupational Therapy***, 29(1), pp. 7-11.

Hackett, K.L. (2013) 'Fighting Fatigue, Book Review', ***Journal of Rheumatology Occupational Therapy***, 28(1), p5.

A.4.2.3Peer reviewed publications under review and in press

Strassheim V, Hackett K.L., Newton J.L. What is known about severe and very severe Chronic Fatigue Syndrome? A scoping review. ***Fatigue Biomedicine Health and Behavior***. (Revised and under review).

Strassheim V., Ballantine R., Hackett, K.L., Frith J., Newton J.L. Understanding severely affected chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): The gravity of the situation. ***Physiotherapy***. (Under review).

A.5 National and International conference abstracts presented during my PhD studies

Hackett K., Forder R, Lendrem D, Hargreaves B, Strassheim V., Gotts, Z., Deary V., Ng W-F, Newton J.L. (2016) Objective improvement in fatigue scores for primary Sjögren's patients receiving a tailored multidisciplinary fatigue intervention in a generic fatigue clinic. **American College of Rheumatology Annual Meeting, Washington D.C., USA.**

(Poster presentation)

Lendrem D., Howard Tripp N., Mariette X., Johnsen SJA., Tarn J., Hackett K., Griffiths B., Mitchell S., Saraux A., Devauchelle, V., Norheim K., Isaacs JD., McMeekin P., Bowman S., Omdal R., Gottenberg J-E., Ng W-F. (2016) Rethinking Primary Sjögren's Syndrome: Stratification by clinical phenotypes to improve understanding of disease pathogenesis, trial design, clinical management and prospective health gains?

American College of Rheumatology Annual Meeting, Washington D.C., USA. *(Oral presentation)*

Hackett K., Forder R, Lendrem D, Hargreaves B, Strassheim V., Gotts, Z., Deary V., Ng W-F, Newton J.L. (2016) Objective improvement in fatigue scores for primary Sjögren's patients receiving a tailored multidisciplinary fatigue intervention in a generic fatigue clinic **CFS/ME Research Collaborative Conference, Newcastle upon Tyne, UK.** *(Poster presentation)*

Strassheim V., Lambson R., Hackett KL., Newton JL. (2016) What is known about severe and very severe chronic fatigue syndrome? A scoping review. **CFS/ME Research Collaborative Conference, Newcastle upon Tyne, UK.** *(Poster presentation)*

Syla D., Sweenie A., Lendrem D., Newton JL., Hackett KL. (2016) A scoping exercise to gauge the incidence of early post stroke fatigue for patients at Newcastle Community Stroke Services. **CFS/ME Research Collaborative Conference, Newcastle upon Tyne, UK.** *(Poster presentation)*

Hackett K., Deary V., Deane K., Kolehmainen N., Newton J., Ng W-F., Rapley, T. (2016) "It isn't pain pure and simple": Experiences of pain and discomfort in primary Sjögren's

syndrome: A qualitative focus group study. **Biomarkers and Targeted Therapeutics in Sjögren's, Oklahoma City, USA.** *(Poster presentation)*

Hackett K., Hargreaves B., Lendrem D., Strassheim V., Gotts Z., Deary V., Ng W-F., Newton JL. (2016) Objective improvement in fatigue scores for primary Sjögren's patients receiving a tailored multidisciplinary fatigue clinic intervention: Provisional findings from the first cohort of patients **Biomarkers and Targeted Therapeutics in Sjögren's, Oklahoma City, USA.** *(Poster presentation)*

Howard Tripp N, Lendrem DW, Tarn J, McMeekin P, Gillespie C, Al-Ali S, Hackett K, Hargreaves B, Mitchell S, Bowman SJ, Price E, Pease CT, Emery P, Lanyon P, Hunter J, Gupta M, Bombardieri M, Sutcliffe N, Pitzalis C, McLaren J, Cooper A, Regan M, Giles I, Isenberg D, Saravanan V, Coady D, Dasgupta B, McHugh N, Young-Min S, Moots R, Gendi N, Akil M, Griffiths B, Isaacs J, Ng WF, on behalf of the UK Primary Sjögren's Syndrome Registry. (2016) Symptom-Based Clinical Phenotyping in Primary Sjögren's Syndrome. **Biomarkers and Targeted Therapeutics in Sjögren's, Oklahoma City, USA.** *(Oral and poster presentation)*

Howard Tripp N, Tarn J, Natasari A, Gillespie C, Mitchell S, Bowman SJ, Price E, Pease CT, Emery P, Andrews J, Lanyon P, Hunter J, Gupta M, Bombardieri M, Sutcliffe N, Pitzalis C, McLaren J, Annie Cooper, Regan M, Giles I, Isenberg D, Saravanan V, Coady D, Dasgupta B, McHugh N, Young-Min S, Moots R, Gendi N, Akil M, Hackett K, Griffiths B, Lendrem D and Ng W-F. (2016) Fatigue in Primary Sjögren's Syndrome is Associated with Lower Levels of Pro-Inflammatory Cytokines. **Biomarkers and Targeted Therapeutics in Sjögren's, Oklahoma City, USA.** *(Poster presentation)*

Howard Tripp N, Lendrem DW, Tarn J, Hackett K, Ng WF. (2016) Clinical Phenotyping in 608 Patients from The United Kingdom Primary Sjögren's Syndrome Registry. **EULAR Congress, London, UK.** *(Poster presentation)*

Hackett KL., Rapley, T., Deane, K., Deary, V., Kolehmainen, N., Newton J., W-F Ng. Identifying key participation barriers for people with primary Sjögren's syndrome to inform a future intervention package using a group concept mapping approach. (2015) **United Kingdom Society of Behavioural Medicine Annual Meeting, Gateshead, UK.** *(Oral presentation)*

Strassheim, V., Lambson, R., Hackett, KL, Newton, JL. The use of pilates style exercise in the treatment of individuals with chronic fatigue. (2015) **CFS/ME Research Collaborative Conference, Newcastle upon Tyne, UK.** *(Poster presentation)*

Hackett, K., Lendrem, D., Rapley, T., Deane, K., Deary, V., Bowman, S., on behalf of the United Kingdom Primary Sjögren's Syndrome Registry, Newton, J. and W-F Ng. (2015) 'Doing Every-Day Life' With Primary Sjögren's Syndrome: Factors Predicting Difficulties Performing Daily Activities and Taking on Life Roles. **American College of Rheumatology Annual Meeting, San Francisco, USA.** *(Poster presentation)*

Hart R., Hackett K., Newton J., Ng W-F., Thompson B. (2015) The F word: Why is talking about fatigue so hard? **American College of Rheumatology Annual Meeting, San Francisco, USA.** *(Poster presentation)*

Hackett K., Newton J., Deane K., Rapley T., Deary V., Kolehmainen N., Ng W-F. (2015) Identifying participation barriers and key intervention targets in an autoimmune disease **College of Occupational Therapists 39th Annual Conference & Exhibition, Brighton, UK.** *(Oral presentation) Prize awarded for best MSc/PhD student oral presentation (UK Occupational Therapy Research Foundation (UKOTRF) Early Researcher Award)*

Hackett K., Rapley T., Kolehmainen N., Deary V., Deane K., Bowman S., Newton, J. Ng W-F. (2015) Identifying potential non-pharmacological intervention targets to improve participation in primary sjogren's syndrome patients and their ability to perform daily activities: a group concept mapping study **EULAR Congress, Rome, Italy.** *(Oral presentation)*

Hackett K., Lendrem D., Frith J., Rapley T., Deary V., Deane, K., Bowman S., Newton, J.L., Ng W-F. (2015) Cognitive symptoms are common in primary Sjögren's syndrome and are associated with anxiety **The 13th International Symposium on Sjögren's Syndrome, Bergen, Norway.** *(Oral presentation)*

Hackett K., Lendrem D., Frith J., Rapley T., Deary V., Deane, K., Bowman S., Newton, J.L., W-F Ng. (2015) Identifying stakeholder informed priority targets for a non-pharmacological intervention package to improve functional capacity: A multi-centre mixed methods study **The 13th International Symposium on Sjögren's Syndrome, Bergen, Norway.** *(Poster presentation)*

Hackett K., Lendrem D., Frith J., Rapley T., Deary V., Deane, K., Bowman S., Newton, J.L., W-F Ng. (2015) Cognitive impairment in primary Sjögren's syndrome **British Society of Rheumatology, Rheumatology, Manchester, UK. (Poster presentation)**

Hackett K.L., Lambson R., Gotts Z.M., Strassheim V., Deary, V. Newton JL. (2015) Identifying and tackling unmet service-user needs in a novel generic fatigue clinic: A group concept mapping study **British Association of CFS/ME Conference, Milton Keynes, UK. (Poster presentation) Poster prize awarded**

Hackett K., Deane K., Deary V., Rapley T., Newton JL., Ng W-F. (2015) Non-pharmacological interventions for primary Sjögren's syndrome: a systematic review of the evidence **EULAR Congress, Paris, France. (Poster presentation)**

Robinson LJ, Hackett K., S Bowman, B Griffiths, Ng W-F., P Gallagher, on behalf of UK Primary Sjögren's Syndrome Registry. (2014) Understanding the gap between subjective symptoms and objective illness markers in primary Sjögren's syndrome **EULAR Congress, Paris, France. (Poster presentation)**

Hackett KL., Deane KHO., Deary V., Newton JL., Rapley T., Ng W-F. (2014) A systematic review of non-pharmacological interventions for primary Sjögren's syndrome **British Society of Rheumatology, Rheumatology, Manchester, UK. (Poster presentation)**

A.6 Prizes and funding awarded during my PhD studies

- Bright Ideas in Health Award, CRESTA Fatigue Team (Team award) (2015)
- United Kingdom Occupational Therapy Research Foundation, Early Researcher Award, (2015)
- BACME (British Association for CFS/ME) Conference, Poster Prize, (2015)
- Newcastle upon Tyne NHS Foundation Trust, Therapy Services, National Recognition Award, (2015)
- United Kingdom Occupational Therapy Research Foundation, Research Career Development Award, (2014-7)
- College of Occupational Therapists, Innovation Award, (2014)
- Arthritis Research UK, Postgraduate Training Fellowship (2013-7)

A.7 Invited oral presentations delivered during my PhD Studies

February 2017: Guest Lecture, Masters in Health Psychology, Northumbria University,
Developing Complex Interventions **Newcastle upon Tyne, UK.**

October 2016: British Sjögren's Syndrome Association AGM and Patient Meeting: The
Academy, The Great Western Hospital, **Swindon, UK.**

October 2016: British Sjögren's Syndrome Association Medical Meeting: The Great
Western Railway Museum, **Swindon, UK.**

September 2016: North East Sjögren's Syndrome Association Meeting: The Freeman
Hospital, **Newcastle upon Tyne, UK.**

June 2016: North East Fatigue Group Education Day: Learning from each other –
clinical and research. Laing Art Gallery, **Newcastle upon Tyne, UK.**

March 2016: Newcastle upon Tyne NHS Foundation Trust Master Class for nurses,
midwives and allied health professionals. Applying for funding: Knowing
the funder, Newcastle University, **Newcastle upon Tyne, UK.**

February 2016: Guest Lecture, Masters in Health Psychology, Northumbria University,
Developing Complex Interventions **Newcastle upon Tyne, UK.**

September 2015: Academic Rheumatology Dept., University of the West of England,
Bristol, UK.

April 2015: Making a difference through clinical research: Nurses Midwives and Allied
Health Professionals Regional Meeting, Great North Museum,
Newcastle upon Tyne, UK

January 2015: Guest Lecture, Masters in Health Psychology, Northumbria University,
Developing Complex Interventions **Newcastle upon Tyne, UK.**

A.8 Summary of future research proposal

This proposal has been awarded funding through an Arthritis Research UK postdoctoral Foundation Fellowship (Grant 21435).

Introduction

Primary Sjögren's syndrome (PSS) patients experience fatigue, pain, sleep disturbances dryness and difficulty performing daily tasks including social/work activities. My PhD research identified; to facilitate independence, PSS patients should be supported to self-manage their symptoms and be informed about their disease. Patients therefore require access to reliable information and evidence-based symptom management programmes. However access to such support is limited for most PSS patients.

This Fellowship follows the MRC guidance for complex intervention research. A self-management intervention will be developed in collaboration with patients and informed by behaviour change techniques. The intervention will be delivered online with the aim of improving patients' skills, knowledge and confidence in self-managing their disease (patient activation) and quality of life (QOL). A feasibility study of the intervention with an integrated process evaluation will be conducted. These results will inform the design and conduct of a future multi-centre trial.

Methods

Work Package 1a: Specifying the intervention content

I will be supported by collaborators/sponsors to develop a PSS self-management, interactive intervention to be delivered via a digital platform (website and linked smartphone application) to deliver information on PSS as well as specific symptom management modules for pain, fatigue, sleep and dryness. The modules will be developed using the MRC Framework which will lead to the development of a specific model/theory that will guide the intervention development. I will utilise patient focus group data (from my PhD), evidence-based intervention components, and BSR/BHPR PSS Guideline recommendations. I have expertise in fatigue interventions and will be supported by sponsors/collaborators with expertise in designing behaviour change, pain, sleep, dryness, education and online interventions.

WP1b: Co-designing the digital tools and user-testing

Regular meetings will occur with patient stakeholders, the research team and web-developers to refine the design, functional elements and usability of the digital self-management tool. Stakeholders will be invited to user-test the tool between meetings and refinements made based on their feedback.

WP2: Feasibility study with process evaluation

A feasibility study will determine both proof of concept/feasibility of the intervention for PSS patients and the protocol for a future multi-centre RCT. Patients will be randomised to receive either usual care plus access to the digital tool or usual care and a booklet. Primary outcomes will include QOL/function. Recruitment, randomisation, follow-up and website engagement rates will be established to inform sample size calculations for the future definitive trial. Further outcomes will include patient activation, health education impact, and symptom scores.

Qualitative interviews with participants will explore experiences of the intervention (e.g. barriers/facilitators to engagement) and trial process. The interviews will inform further enhancements to the digital tool and design of a future multi-centre trial.

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